Epilepsy & Behavior 22 (2011) 342–345

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Survivors and nonsurvivors of very prolonged status epilepticus

Frank W. Drislane [a,*], M. Raquel Lopez [b], Andrew S. Blum [c], Donald L. Schomer [a]

[a] Department of Neurology, Harvard Medical School, and Comprehensive Epilepsy Center, Beth Israel Deaconess Medical Center, Boston, MA, USA
[b] Department of Neurology, University of Miami, Miami, FL, USA
[c] Comprehensive Epilepsy Program, Rhode Island Hospital, Brown Medical School, Providence, RI, USA

ARTICLE INFO

Article history:
Received 23 May 2011
Revised 7 July 2011
Accepted 15 July 2011
Available online 16 August 2011

Keywords:
Status epilepticus
Nonconvulsive status epilepticus
Prognosis
Predictive factors
Coma
Intensive care unit
Treatment
Futility

ABSTRACT

Several studies have shown reliable predictive factors for outcome in status epilepticus (SE), especially etiology and presentation in coma. Duration of SE is predictive, but probably only in the first few hours, and there have been many reports of patients treated successfully for SE lasting many days or weeks. Nevertheless, there are many other patients with SE treated for prolonged periods without success, sometimes apparently futilely. We compared clinical features of 10 survivors of prolonged SE with those of a matched cohort treated for similarly prolonged episodes but unsuccessfully, looking for exceptions to known predictive factors. Multiple medical problems (i.e., etiologies) and coma on presentation were confirmed as predictors of a poor outcome. Analysis of individual exceptions to these predictors showed that age, overall background health, and family input on the value of prolonged treatment, on the one hand, and earlier epilepsy plus rapid and accurate diagnosis and treatment, on the other, contributed to results different from what would have been expected.

1. Introduction

Predictors of survival in status epilepticus (SE) have been determined in several studies of large case series [1–5]. In nearly all, etiology is the primary predictor. Indeed, when SE has an acute symptomatic cause (e.g., encephalitis, hemorrhage, major stroke) mortality can be 30–50% [6–8]. Presentation in coma (often related to the severe etiologies) is also a strong predictor of a poor outcome [4,5].

Other poor prognostic factors may include older age [2,3,9], nonconvulsive SE [10], and duration of SE (also often related to severe etiologies) [1]. After the first hour or so, however, duration of SE alone is not a significant predictor of outcome, independent of etiology or presentation in coma [3,5], and some patients with very prolonged SE survive [11–14]. Many patients with SE have had prolonged treatment courses, some successful and others futile, and it is not completely clear which patients should be treated aggressively and for how long.

In prolonged SE, no prognostic factor is perfect in predicting outcome, and not all patients follow the expected course. Believing that it might be important to examine apparent exceptions to predicted outcomes, we reviewed individual case histories of patients with particularly prolonged episodes of SE, seeking details of their clinical courses that would predict utility or futility of prolonged treatment.

2. Methods

Patients were selected from the data in an earlier study on the effects of the duration of SE on outcome in 119 patients [5]. We reviewed clinical and EEG details of the hospital courses of the 10 survivors with the longest duration of SE and of a matched cohort of patients treated the longest, but unsuccessfully. The comparison group of nonsurvivors included 11 patients because the patients with the 10th and 11th longest episodes of SE had, as best could be determined, identical durations of SE. Patients with SE caused by anoxia were excluded. The project was approved by the institutional review board of Beth Israel Deaconess Medical Center.

All patients were diagnosed as having both clinical deficits and EEGs showing ongoing seizures, with either brief, intermittent evolving electrographic seizures or prolonged but rhythmic and rapid epileptiform discharges, either focal or generalized. Clinical records confirmed an abnormal mental status or focal neurological deficit lasting at least 30 minutes, including at the time of the EEG recording. The onset of SE was ascertained at the beginning of clear clinical seizure activity or from a sudden and major decline in neurological function (without interval recovery) before the first EEG showing ongoing seizures. Cessation of SE was determined by clinical recovery, if this occurred rapidly, or from EEG evidence.

* Corresponding author at: Department of Neurology, KS 479, Beth Israel Deaconess Medical Center, 330 Brookline Avenue, Boston, MA 02215, USA. Fax: +1 617 667 7919.
E-mail address: fdrislan@bidmc.harvard.edu (F.W. Drislane).

1525-5050/$ – see front matter
doi:10.1016/j.yebeh.2011.07.013

We compared etiology, age, history of epilepsy, epilepsy or seizures as the cause of the current episode of SE, presence of multiple medical problems (sepsis or infection, as with HIV; hepatic failure; renal failure necessitating dialysis; recent major surgery; diabetes requiring increased insulin; cancer; or gastrointestinal bleeding or severe cardiopulmonary illnesses [such as myocardial infarction, respiratory failure, congestive failure or hypotension] requiring treatment independent of the neurological disease), level of consciousness on diagnosis of SE (presentation in coma vs lethargy, confusion, or stupor), generalized or focal clinical and EEG features of the SE, and number of anticonvulsants used in treatment. We also looked for clinical details that might influence the outcome in those patients whose courses did not follow predicted patterns.

Prognostic factors and outcome were compared statistically in 2×2 tables, with χ^2 or Fisher's exact test, for significance of the factors in predicting a poor outcome. Statistical results were not controlled for multiple comparisons because of the relatively small number of patients in the study and its exploratory nature.

3. Results

Causes of prolonged, refractory SE were many and diverse, including strokes, tumors, encephalitis, and (more than others) multiple medical problems, including infection, organ failure, and vascular disease, often in the postoperative setting. No single etiology was predominant in either group. Patients with anoxia were excluded.

The 10 survivors had episodes of SE lasting at least 4 days (range: 4–59 days, median: 5 days). Those treated unsuccessfully were treated for at least 5 days (range: 5.5–17 days, median: 7.5 days). Between the two groups, there was no significant difference in generalized or focal epileptiform discharges on the EEG during SE or in numbers of anticonvulsants used (see Table 1). Most patients in both groups had generalized epileptiform discharges on their EEGs during SE, but many had focal abnormalities clinically or on scans.

Survivors were slightly younger on average, but the oldest patient in the series was a 96-year-old woman who survived with a reversible medical illness (gastrointestinal bleeding and a urinary tract infection). Four patients in each group had earlier histories of epilepsy, but four survivors (and no nonsurvivors) had epilepsy that was considered a major contribution to their having SE; this difference between the two very small groups did not reach statistical significance.

The presence of multiple medical problems or coma on presentation was a strong predictive factor for a poor outcome ($P<0.01$, for each factor). All patients who died had multiple medical problems or presented in coma, or both. The two patients who died without presenting in coma had major medical problems; one was an 85-year-old woman whose family decided to limit treatment. Three patients survived despite the presence of coma, multiple medical problems, or both. Case histories of these exceptions are detailed below to illustrate some individual clinical features that might be used to refine predictions of who will survive despite prolonged episodes of SE.

Table 1
Prognostic factors for survivors and non-survivors of prolonged status epilepticus.

	Survivors	Non-survivors	
Age (mean, years)	60	67	N.S.
Duration (median, hours)	120	168	(NS[a])
Presented in coma	2	9	$p<0.01$[b]
Multiple medical problems	2	9	$p<0.01$[b]
Epilepsy as the primary cause	4	0	$p<.1$[b]
History of epilepsy	4	4	N.S.
Generalized epileptiform discharges on EEG	9	8	N.S.

[a] Not significant in a larger study, when controlled for etiology and presentation in coma.
[b] Fisher's exact test; 2-tailed.

3.1. Case studies

Two patients not presenting in coma died.

1. A 43-year-old man with HIV infection and history of cytomegalovirus retinitis was admitted with lethargy and confusion, without any history of a clinical seizure. Worsening of his mental status in the hospital on day 10 led to an EEG showing ongoing epileptiform discharges indicative of nonconvulsive status epilepticus (NCSE). He was treated with phenytoin intravenously, but (without more intensive treatment) seizures continued for more than 1 week (180 hours). He had no clinically evident convulsions or obvious seizures during the hospitalization. On day 13, a right temporal lobe brain biopsy showed evidence of toxoplasmosis. Although the SE appeared to resolve eventually, he died on hospital day 26 from infectious complications of his HIV disease. He had the favorable factors of relative youth and presenting not in coma, but the multiple medical problems were likely determinant of his course.
2. An 85-year-old woman without an earlier history of seizures had a single generalized convulsion prompting admission. After the seizure, she was awake but remained confused. On admission, an EEG showed ongoing NCSE. She had numerous medical problems, including several metabolic abnormalities, a probable urinary tract infection, and a remote history of metastatic thyroid cancer. Despite treatment with intravenous phenytoin, the EEG continued without much change over 132 hours, and she became progressively less alert. On the sixth hospital day, the family decided to withdraw medical care, and she died later that day. The lack of coma on diagnosis was a favorable prognostic factor, but the patient was elderly and had chronic illnesses and multiple medical problems. This contributed to her family's wish to avoid treatment other than comfort measures.

Three patients survived who would have been predicted to die by usual prognostic factors.

3. A 47-year-old woman with chronic renal failure had had several isolated generalized convulsions at home during the 2 weeks before admission. She also had intestinal bleeding and a likely urinary tract infection, and was admitted in coma. An EEG showed ongoing epileptiform seizure activity. She was treated with phenytoin, valproic acid, phenobarbital, lorazepam, and hemodialysis. EEG evidence of ongoing seizures lasted 148 hours, but, with treatment, she recovered eventually. On the 10th hospital day, continued impairment of mental status was thought more likely due to the medications she had received. Gradual withdrawal of some medications led to her being alert progressively and fully after about a week, and she was transferred to a rehabilitation hospital. Unfavorable prognostic factors included admission in coma and multiple medical problems. Her age of 47 and the aggressive treatment of the underlying illnesses were key to her survival. The early and prompt diagnosis of SE on admission was likely to have helped.
4. A 24-year-old graduate student had had a few possible seizures at age 11 but had not been on anticonvulsant medications in several years. He had a convulsive seizure at home and two more convulsions in the emergency room and was admitted, comatose. Treatment comprised lorazepam, phenytoin, phenobarbital, and midazolam, with intermittent success for 5 days, but with recurrent frequent seizures and NCSE after that. The EEG showed seizures over the next 8 days. An extensive workup, including brain biopsy, found no cause. He remained on pentobarbital and numerous other medications from days 6 to 59 of his hospitalization, with electrographic status epilepticus recurring with each