Journal of Clinical Neuroscience 21 (2014) 1915–1919

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

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

Clinical Study

Etiology and prognosis of non-convulsive status epilepticus

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ARTICLE INFO

Article history:
Received 14 November 2013
Accepted 8 March 2014

Keywords:
Etiology
Non-convulsive status epilepticus
Prognosis

ABSTRACT

Although non-convulsive status epilepticus (NCSE) is an important type of epilepsy, it is not often recognized. In order to analyze the clinical characteristics and outcome in patients with NCSE, we examined the medical records of patients with NCSE admitted to the Seoul National University Hospital between June 2005 and October 2008. The clinical details and electroencephalography records of 34 adult NCSE patients (aged over 16 years) were collected. Their mean age was 47 years (standard deviation 20 years, range, 16–87 years), and 20 were female. Twenty-seven patients (79.4%) showed decreased awareness with acute onset, and seven (20.6%) were obtunded or comatose. Ten patients (29.4%) had a history of epilepsy, and four (11.8%) had a history of stroke. NCSE was etiologically attributed to acute medical or neurological problems in 25 patients (73.5%), was cryptogenic in three (8.8%), and was secondary to underlying epilepsy in six (17.7%). Acute symptomatic etiology was associated with poor recovery ($p = 0.048$), with all unresponsive patients in this acute symptomatic group. Eight (23.5%) of the 34 NCSE patients did not recover or died, whereas nine (26.5%) recovered. Our study shows that the presence of acute symptoms or central nervous system infection is associated with poor outcome, suggesting that a high level of vigilance is required to identify and prevent complications.

1. Introduction

Status epilepticus (SE) can be divided into generalized convulsive status epilepticus (GCSE), which is a major neurological and medical emergency associated with significant morbidity and mortality [1–3], and non-convulsive status epilepticus (NCSE), which is usually characterized by some degree of clouding of consciousness [4,5]. GCSE is associated with a mortality rate as high as 22% [1], and NCSE constitutes approximately 25% of SE patients [6,7], persisting in 14% of patients after control of GCSE [8]. The prevalence of NCSE is approximately 8% in all comatose patients with no clinical signs of seizure activity in the intensive care unit [9]. Although both conditions require prompt diagnosis and intervention [10,11], the clinical features of NCSE are subtle and not specific, so it is usually underdiagnosed and mistaken for behavioral or psychiatric disturbances [5].

NCSE is defined as a state of seizures without convulsions, lasting for more than 30 minutes associated with continuous or near continuous epileptiform discharges on electroencephalography (EEG) [4,6,12]. On the basis of ictal EEG patterns it has been subcategorized into absence SE, with predominantly symmetrical synchronous ictal discharges, and complex partial-status epilepticus, with continuous or rapidly recurring complex partial seizures [13].

The potential for NCSE to cause direct brain injury is controversial [11,14–16]. Some studies have described NCSE as having high mortality and high morbidity [17], but others report NCSE as a benign condition that does not require aggressive therapy [18,19]. The etiology, diagnosis, treatment and prognosis of NCSE remain controversial [4,13,20–24]. The prognosis depends not only on detailed assessment of the type of NCSE but also on the level of consciousness [5,25]. Good outcome might be associated with early and appropriate treatment [26,27]. In this study, we attempted to assess the etiology and prognosis of NCSE, and to identify prognostic factors.

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http://dx.doi.org/10.1016/j.jocn.2014.03.018
0967-5868/

2. Methods

We screened the computerized database of the Seoul National University Hospital for patients with NCSE during the period June 2005 to October 2008. All patients showed an unexplained decreased level of consciousness or altered mental state. The six clear-cut EEG criteria for NCSE proposed by Kaplan [12] were used: (1) frequent or continuous focal electrographic seizures, with ictal patterns that wax and wane with change in amplitude, frequency, and/or spatial distribution; (2) frequent or continuous generalized spike-wave discharges in patients without a previous history of epileptic encephalopathy or epilepsy syndrome; (3) frequent or continuous generalized spike-wave discharges, which showed significant changes in intensity or frequency (usually a faster frequency) when compared to baseline EEG, in patients with an epileptic encephalopathy or epilepsy syndrome; (4) periodic lateralized epileptiform discharges (PLED) or bilateral periodic epileptiform discharges (BIPED) that occurred in patients in coma in the aftermath of a generalized tonic-clonic SE (subtle SE); (5) EEG patterns that were less easy to interpret including frequent or continuous EEG abnormalities (spikes, sharp-waves, rhythmic slow activity, PLED, BIPED, generalized periodic epileptiform discharges, triphasic waves) in patients whose EEG showed no previous similar abnormalities, in the context of acute cerebral damage (such as anoxic brain damage, infection, trauma); and (6) frequent or continuous generalized EEG abnormalities in patients with epileptic encephalopathies in whom similar interictal EEG patterns were seen, but in whom clinical symptoms were suggestive of NCSE. The administration of benzodiazepine during EEG recording and the subsequent cessation of ictal discharges and improvement of mental status were not necessary for diagnosis. NCSE cases following a single brief convulsion were included, but patients who presented with GCSE and who were later found to have NCSE were excluded.

Electronic medical records were reviewed for variables such as symptom description, treatment, acute medical problems, and complications in treatment or clinical outcome. Other information included age, sex, seizure history, stroke, cognitive impairment, brain tumor or intracranial surgery, and neuroimaging data. Mental status was measured at the time of admission or at the initial neurology consultation. Mental impairment was considered to be mild if the patient was awake but confused, and severe if the patient was obtunded or comatose.

Etiologies were categorized into the following three major groups: (1) epileptic, with patients having a history of seizures but no other acute medical problem; (2) cryptogenic, with patients with no history of seizures and absence of any other acute problems; and (3) acute symptomatic, with patients having an acute medical or neurological problem. Patients who had a pre-existing seizure history plus acute medical problems were included in the acute symptomatic etiology group. The acute symptomatic group included those with head injury in the 4 weeks prior to presentation, those with acute ischemic stroke within 7 days of observed alteration in mental state, and those experiencing a period of hypoxia, neuroinfection, severe systemic infection, hyponatremia (<130 mEq/L plasma sodium level), hypoglycemia (<50 mg/dl plasma glucose level) or other electrolyte disturbances (in calcium, phosphors, potassium, or magnesium). Medications at admission, duration from time of symptom onset to start of medication, the duration of NCSE, and mental state on discharge or at 30 days after admission were examined. Morbidity was defined as any acute complication, medical or neurological, during admission. Unresponsive patients were defined as those who had no change in their condition or had died. Partial improvement was defined as an improvement in both the level of consciousness and functional performance of at least some of the activities of daily life.

2.1. Statistical analysis

We determined how the primary variables correlated with mortality and morbidity, and how the characteristics of the primary variables differed among the different etiologic groups. Categorical variables were compared using the *t*-test or Fisher's exact test. Values of $\leqslant 0.05$ for these tests were considered to be statistically significant.

3. Results

3.1. Clinical characteristics

A total of 34 patients aged over 16 years were recruited. All the patients in this study presented decreased mental status. The mean age was 47 years (range 16–87), and 14 (41.2%) were male. Confusion was the characteristic symptom in 27 patients (79.4%), and 13 patients (38.2%) had a neurological history. Ten patients in this group had a history of seizures (Table 1). Generalized spike and wave discharges were shown in 12 patients, PLED in 11 patients and BIPED in 11 patients.

3.2. Etiology

NCSE was attributed to acute medical or neurological problems in 25 patients (73.5%) but was cryptogenic in three (8.8%) and/or associated with underlying epilepsy in six (17.7%). Fifteen patients had a single acute neurological problem and five had a single medical problem, whereas both acute medical and neurological problems were present in another five patients. In those patients with acute symptomatic etiology, the leading cause was central nervous system (CNS) infection followed by metabolic causes and systemic infections (Table 2).

3.3. Treatment

All patients in the NCSE group received at least one antiepileptic drug, but there was no standard treatment. Twenty-seven patients (79.4%) were loaded with a first-line antiepileptic drug (phenytoin, valproic acid, oxcarbazepine, or combination of any of these medications). The mean duration from symptom onset to treatment was 15.9 days (range 1–111 days) with the mean duration from admission at our hospital to treatment being 3.5 days (range 1–38 days).

3.4. Outcome

Eight (23.5%) of the 34 patients with NCSE did not recover or died, nine (26.5%) returned to normality, and partial improvement was seen in 17 (50%) (Table 3). All unresponsive patients were in the acute symptomatic group, two with CNS infection, two with severe systemic infection, one with subdural hemorrhage following head injury, one with stroke, one with hypoxia, and one with hypoglycemia due to insulinoma (Table 4). Acute symptomatic etiology was also associated with poor outcome ($p = 0.048$). The rates of mortality and poor outcome for each etiology and complication were assessed. Mortality was greatest in patients with CNS infections ($p = 0.03$). Patients with metabolic problems were more likely to have a favorable outcome ($p = 0.05$). Complications during NCSE occurred in 11 patients, with pneumonia the most common problem. Complications were more likely to occur in the acute symptomatic group (91%) than in the epilepsy group (9%). Poor prognosis was not statistically associated with the duration of NCSE at 37.7 days (standard deviation 5.6, range 3–170) or severe