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The yield of routine electroencephalography in the detection of incidental nonconvulsive status epilepticus – A prospective study

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HIGHLIGHTS

- Prospective study on the incidence of NCSE.
- Half of NCSE unsuspected to treating physicians.
- Unsuspected NCSE mostly in patients without significant reduction of consciousness.

ABSTRACT

Objective: Diagnosis of NCSE is challenging, because the clinical presentation ranges from minimally altered mental status to coma without tonic–clonic activity. According to the largest retrospective study to date the incidence of NCSE is about 0.2%.
Methods: We prospectively investigated electroencephalography (EEG) recordings of 2514 consecutive patients that were referred to the Electrophysiology Unit of Department of Neurology, Vienna General Hospital between November 2009 and February 2011 (i.e. 16 months).
Results: The incidence of NCSE in our study population was 0.8%, i.e. the EEG of 19 patients fulfilled the criteria of NCSE. In 53% of these patients the NCSE was not suspected by treating physicians. A severely reduced level of consciousness was found in 78% of patients with a suspected NCSE and in 30% of patients with an unsuspected NCSE, although the results were not statistically significant ($p = 0.081$). The delay between the admission to the hospital and diagnosis ranged between 0 and 51 days.
Conclusions: NCSE was an unsuspected finding in more than half of the patients. Consciousness was severely impaired in only one third of these patients.
Significance: These results highlight the importance of urgent EEG for the diagnosis of NCSE in patients even without significant impairment of consciousness.

1. Introduction

Diagnosis of NCSE is challenging, because the clinical presentation ranges from minimally altered mental status to coma without tonic–clonic activity (Jirsch and Hirsch, 2007). Data about morbidity and mortality rates associated with NCSE vary considerably (Cockerell et al., 1994; Young et al., 1996).

Previously, a large retrospective study reported an incidence of NCSE of 0.2% (Shneker and Fountain, 2003). Most recently, the incidence of NCSE was prospectively investigated in 49 of 290 patients admitted to a palliative care unit showing signs of confusion or delirium and/or a reduction in their level of consciousness. NCSE was suspected clinically in 22 of these patients, and epileptic activity could be confirmed in 15 (5.2%) of 290 patients (Lorenzl et al., 2010).

In a series of 45 patients with NCSE in a tertiary referral center the referring clinicians suspected NCSE in 36 patients (80%). The diagnosis was more likely to be suspected in patients with a previous history of epilepsy (Haffey et al., 2004). Conversely, NCSE was less likely to be suspected in patients who appeared to be alert and relatively cooperative (Haffey et al., 2004). In another study the usefulness of clinical features in selecting patients with suspected NCSE for urgent EEG was investigated. The authors concluded that the combined diagnostic sensitivity of remote risk factors for seizures and ocular movements abnormalities was 100% (Husain et al., 2003).

The diagnosis of NCSE may be missed in the emergency room when the behavioral or cognitive changes from baseline are ascribed to other causes, including intoxication, postictal state, preexisting psychiatric conditions, or mental retardation (Kaplan, 1999). The delay in diagnosis of NCSE may range from 3 h to 28 days, with a mean of 3 days (Audenino et al., 2003). A previous study showed that NCSE was the second most common reason for

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ordering an EEG in the emergency room and that an urgent EEG contributed significantly to the diagnosis and management of NCSE (Praline et al., 2007).

We conducted an analysis of routine EEGs performed between November 2009 and February 2011 to present prospective data about (1) the incidence of NCSE among patients in a tertiary referral center, (2) the delay from admission to the documentation of NCSE during EEG and (3) the portion of patients with NCSE in whom the diagnosis was suspected.

2. Patients and methods

Between November 2009 and February 2011 all consecutive patients referred to an EEG at the Department of Neurology or any Intensive Care Unit at the Vienna General Hospital were screened for NCSE during the EEG recording. All recordings were reviewed by two EEG-board certified authors (E.P. and S.A.-W.). The EEG was performed with a commercially available digital EEG system (alpha-trace 32-channel digital EEG record, B.E.S.T. Medical Systems, Vienna) for an average of 30 min. The EEG electrodes were placed according to the extended International 10–20 system with additional fronto-temporal electrodes (FT9/FT10).

We adopted the criteria for definition of NCSE proposed by Young et al. (1996) and modified by Chong and Hirsch (2005): at least one of the following three primary criteria had to be fulfilled. Primary criteria were (1) repetitive generalized or focal spikes, sharp waves, spike-and-wave or sharp-and-slow wave complexes at a frequency of $\geqslant$3/s; (2) repetitive generalized or focal spikes, sharp waves, spike-and-wave or sharp-and-slow wave complexes at a frequency of <3/s and the secondary criterion; or (3) sequential rhythmic, periodic, or quasi-periodic waves at $\geqslant$1/s and unequivocal evolution in frequency (gradually increasing or decreasing by at least 1/s, e.g. from 2 to 3/s), morphology, or location (gradual spread into or out of a region involving at least two electrodes). Evolution in amplitude alone is not sufficient. Change in sharpness without other change in morphology is not adequate to satisfy evolution in morphology.

The secondary criterion was the following: significant improvement in clinical state or appearance of previously-absent normal EEG patterns (such as a posterior dominant rhythm) temporally coupled to acute administration of a rapidly-acting antiepileptic drug (AED). Resolution of the "epileptiform" discharges leaving diffuse slowing without clinical improvement and without appearance of previously-absent normal EEG pattern would not satisfy the secondary criterion.

If the EEG fulfilled the criteria of NCSE the video was screened to determine clinical correlates. Only the EEGs without clinical signs in the co-registered video were considered for further analyses (Young et al., 1996). The level of consciousness during the EEG recording was documented and divided into four categories: alert, somnolent, stuporous and comatous.

Clinical data were gathered from chart review, EEG reports, discharge summaries, and resident sign-out notes. Baseline demographic data (age, gender) and past medical history (including epilepsy, stroke, brain tumor and neurosurgical procedures) were assessed.

The statistical analysis of the data was performed using commercially available statistical software (SPSS 17.0; Chicago, IL). Data are presented as median ± standard deviation (SD) or percentages. Demographic and clinical characteristics of patients with suspected and unsuspected NCSE were compared using chi-square tests for ordinal and two-sided students' *t*-tests for metrical data. The level of significance was set to $p < 0.05$. Due to the small number of patients with NCSE we put caution on the interpretation of these statistical analyses.

3. Results

Two thousand five-hundred and fourteen consecutive patients were referred to the EEG during the observation period of 16 months. Of these 352 patients (14%) from Intensive Care Units

Table 1
Demographic and clinical characteristics of patients with NCSE.

Sex	Age	Comorbidities	Main comorbidity	GCSE on admission	Days to EEG[a]	Imaging	Presentation during EEG	Clinical outcome	Seizure history
M	57	4	Acute myeloid leucemia	Yes	3	Ischemic lesion, hygroma	Comatous	Dead	Positive
F	70	8	Toxic hepatopathy	Yes	2	–	Comatous	Dead	Positive
M	52	4	Intracranial hemorrhage	No	5	Intracranial hemorrhage	Comatous	Discharged	Negative
F	72	5	Atrial fibrillation	Yes	0	–	Stuporous	Dead	Negative
M	48	1	Lymphoma	Yes	24	Tumor basal ganglia	Comatous	Dead	Negative
F	25	3	Lennox-Gastaut Syndrome	Yes	2	–	Comatous	Discharged	Positive
F	58	1	Severe brain trauma	Yes	2	–	Comatous	Discharged	Negative
M	52	3	Liver cirrhosis	Yes	0	–	Comatous	Discharged	Positive
M	74	1	Multiple meningeomas	No	8	Multiple meningeomas	Somnolent	Dead	Negative
F	83	2	Meningeoma	Yes	1	Occipital post-resection defect	Somnolent	Dead	Positive
M	61	2	Oral squamous cell carcinoma	No	1	Thalamic ischemic lesion	Comatous	Discharged	Negative
F	66	3	Brain metastases of unknown origin	No	22	Brain metastases	Somnolent	Dead	Positive
F	43	2	Meningeoma	Yes	2	Frontal post-resection defect	Alert	Discharged	Negative
M	74	5	Lung carcinoma	Yes	12	Brain metastases	Somnolent	Discharged	Positive
F	83	7	Osteoporosis	Yes	0	–	Somnolent	Discharged	Negative
F	62	3	Glioblastoma	Yes	8	Glioblastoma	Somnolent	Discharged	Positive
M	73	3	Renal insufficiency	No	10	Ischemic lesion caudate nucleus	Somnolent	Discharged	Negative
F	77	2	Aortic aneurysma	No	51	–	Comatous	Discharged	Negative
M	57	1	Astrocytoma	No	6	Parietal post-resection defect	Somnolent	Discharged	Positive

GCSE = generalized convulsive status epilepticus.
[a] EEG documenting the NCSE.