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The electroclinical spectrum, etiologies, treatment and outcome of nonconvulsive status epilepticus in the elderly☆

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ABSTRACT

Background: Nonconvulsive status epilepticus (NCSE) in the elderly is particularly difficult to diagnose, mainly due to subtle clinical manifestations and associated comorbidities. The recently validated electroencephalography (EEG) diagnostic criteria for NCSE and the proposed operational classification of status epilepticus provide tools that can allow an earlier diagnosis and better management of NCSE in this age group, possibly contributing to reduce its high mortality.
Material and methods: we used these tools to identify and characterize a cohort of elderly (>60 year-old) patients admitted at our institution in a 3-year period; the video-EEG and clinical files of the patients fulfilling EEG diagnostic criteria for NCSE were reviewed, being in this study described their electroclinical spectrum, etiologies, treatment, inhospital mortality, and status epilepticus severity score (STESS).
Results: Fourty patients (23 women; mean age 76.6 years) were identified. Although dyscognitive NCSE associated with >2.5 Hz of epileptiform discharges (ED) was the most frequent electroclinical phenotype, this was quite heterogeneous, ranging from patients with aura continua to patients in coma, associated with frequent ED or rhythmic slow activities. Acute symptomatic (45%) and multifactorial (27.5%) etiologies were the most common, and associated with the worst prognosis. There was a trend to use newer antiepileptic drugs in the early steps of NCSE treatment. The inhospital mortality was high (22.5%) and predicted by STESS scores ≥3.
Conclusion: In the elderly, NCSE has heterogeneous electroclinical phenotypes and etiologies. In spite of the treatment limitations conditioned by the comorbidities, more aggressive treatments could be justified to reduce mortality in patients with high STESS scores.

1. Introduction

Epidemiological studies have consistently demonstrated that the incidence and prevalence of seizures, including nonconvulsive status epilepticus (NCSE), are highest in the elderly [1–3]. In this age group, the clinical diagnosis of NCSE is particularly challenging, mainly due to subtle motor manifestations and because the consciousness impairment that dominates the clinical picture may be attributed to metabolic/infectious/toxic disorders and/or underlying dementia, all commonly found in the elderly [4,5]; in this scenario, electroencephalography (EEG) emerges as the only diagnostic tool that allows the definite diagnosis of NCSE. In spite of the preponderant role of EEG in NCSE diagnosis, the few studies that exclusively evaluated NCSE in the elderly [6–11] used different EEG terminologies and criteria, or are scarce in the description of the EEG findings that lead to its diagnosis; moreover, the heterogeneous outcome measures and electroclinical criteria used to classify different types of NCSE contribute to the difficulties in making evidence-based management guidelines for this condition.

The systematic application to each individual patient with suspected NCSE of the recently proposed EEG unified terminology [12], validated EEG criteria for diagnosing NCSE [13], a stepwise approach to classify status epilepticus (SE) [14], and specific outcome scales [15,16] could overcome those limitations, facilitating the communication between physicians and allowing data comparison between different studies. In this study, hoping to contribute to a more robust knowledge about the electroclinical features, etiologies, treatment and outcome of NCSE in

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the elderly, we used this systematic approach and criteria to describe a large cohort of elders with NCSE.

2. Material and methods

We identified all consecutive patients admitted at our hospital between January 2012 and December 2015 in which the diagnosis of NCSE was made. Their video-EEG files (minimum 1-hour duration; 10/20 EEG system) were reviewed by the same neurophysiologist (NC), being only included in this study patients older than 60 years with an altered mental status or symptoms lasting at least 10 min associated with electroclinical findings fulfilling the recently validated Salzburg consensus criteria for NCSE [13]; patients identified in the intensive care unit (ICU) and with hypoxic–anoxic or epileptic encephalopathy were excluded. The clinical files of eligible patients were reviewed, with demographic, clinical, electrographic, etiological, and outcome data obtained retrospectively and registered in a dedicated database. For each patient, we considered: a previous diagnosis of epilepsy (considered controlled if seizure-free for the last 12 months) or dementia made by a neurologist, the clinical suspicion of NCSE before EEG confirmation; the presence of an isolated convulsive seizure during the course of NCSE, the results of the laboratory and brain neuroimaging studies, the drugs used to NCSE treatment, the status epilepticus severity score (STESS) [15], and the inhospital mortality. Given the preponderant role of the electroclinical features for the diagnosis and classification of NCSE, the data obtained by reviewing the video-EEG files of each patient were registered as follows: type (spikes, sharp-waves, poly spikes, sharp-and-slow-wave complexes), location (affected brain lobe), and higher frequency (in a 10-second epoch) of the epileptiform discharges (ED) or rhythmic slow activities; the presence of EEG patterns with typical ictal spatiotemporal evolution, and their association (or not) with subtle clinical findings; and the use and response (electrographic, clinical or both) to intravenous (IV) antiepileptic drugs (AED) administered during video-EEG. Based on these findings, a definite diagnosis of NCSE was made if: more than 25 ED per 10-second epoch (ED > 2.5 Hz) - criteria A; or ED ≤ 2.5 Hz (criteria B) or rhythmic delta/theta activity (>0.5 Hz; criteria C) and one of the following secondary criteria: 1. EEG and clinical improvement after IV AED (evaluated within 10 min after its application); 2. subtle clinical ictal phenomena during the EEG patterns; and 3. typical ictal-EEG spatiotemporal evolution. According to the recently proposed classification of SE, NCSE was classified electroclinically and etiologically [14].

This is a retrospective non-invasive study, which do not require ethics committee approval and informed patient consents according to the Portuguese Law on research.

3. Results

3.1. Patient demographics and clinical findings at presentation

We identified 40 patients (23 women) fulfilling the inclusion criteria, 27 in the emergency department and 13 at the ward. The youngest patient was 60 years old and the oldest 92 years old, with an average age of 76.6 years. Eleven patients had a previous diagnosis of epilepsy, focal symptomatic in 8 (4 vascular, 2 posttraumatic, 2 associated with Alzheimer's disease), unknown in the others, being 45.5% (5/11) controlled; 16 patients had a diagnosis of dementia. Confusional states (22/40) and consciousness level fluctuations (13/40), occasionally associated with subtle motor manifestations (nystagmoid eye movements, subtle myoclonic jerks), were the most frequent reasons for ordering an EEG; less frequently (5/40) it was requested for unexplained visual or language symptoms, or after a first seizure. Before EEG confirmation, the clinical diagnosis of NCSE was only considered in 11 patients, all with an isolated convulsive seizure at presentation (which occurred in 17 patients) or with a history of epilepsy.

3.2. Electroclinical phenotypes

The electroclinical criteria that allowed the definitive diagnosis of NCSE are summarized in Table 1. These were present at the initial video-EEG in 38 patients, and in subsequent video-EEGs (3–4; average 3.5) in 2. Although a minimum of 10 consecutive seconds with ED or rhythmic slow activities fulfilling criteria A to C was required to consider the diagnosis of NCSE, the video-EEG recordings of these patients were highly dynamic, showing fluctuating patterns that could be intermixed with typical ictal-EEG patterns associated or not with minor motor signs, and with variable responses to IV AEDs, explaining why more than one secondary criteria could be present in the same patient. In this way, 24 patients had typical ictal spatiotemporal evolutions on EEG, in 18 associated with minor motor manifestations, mostly localized to oculocephalic region (eye/head deviations, masticatory automatisms) or lateralized to the distal extremities (subtle clonic jerks), corresponding to electroclinical seizures. Intravenous diazepam was administered during video-EEG in 12 patients, leading to a marked decrease of the ED, ictal-EEG patterns, electroclinical seizures, and clinical improvement in 7, contributing to the definitive diagnosis of NCSE; and only to an EEG response, without full clinical recovery, in the other 5 patients, in these cases with the definitive diagnosis of NCSE made according to other criteria. Based on the review of the video-EEG files, NCSE was classified as NCSE with coma in 5 patients; and focal NCSE without coma in 35 patients, 33 with impaired consciousness (dyscognitive), 1 with visual aura continua, and 1 with aphasic SE. In the patients with dyscognitive NCSE, the EEG criteria that allowed a definitive diagnosis of NCSE were criteria A, present in 16 out of 33 patients, criteria B (13/33) and criteria C (4/33); although the great majority of these patients (28/33) showed epileptiform/rhythmic slow activities located in the frontotemporal regions, in 5 these were in more posterior brain regions. In the 5 patients diagnosed as NCSE with coma, 2 fulfilled criteria A and 3 criteria B, with 4 presenting epileptiform abnormalities located in the frontotemporal regions, in the other more posterior. The patient with aphasic NCSE had ED < 2.5 Hz in the left frontotemporal region, with a rapid clinical and electrographic response to IV diazepam; and the patient with visual aura continua had rhythmic slow activities located in the posterior brain regions, with evolution in patterns corresponding to visual symptoms.

3.3. Etiologies

All patients were submitted to an extensive laboratorial evaluation including hemogram, ionogram, renal/hepatic/thyroid function, toxic

Table 1
Electroclinical criteria that allowed the diagnosis of NCSE. A definite diagnosis of NCSE was made if: more than 25 epileptiform discharges (ED; spikes, sharp-waves, poly spikes, sharp-and-slow-wave complexes) per 10-second epoch (criteria A); or if criteria B or C were present with at least one of the secondary criteria (1 to 3). Since the EEGs in these patients were highly dynamic, more than one secondary criteria could be present in each patient. *if only EEG but no clinical improvement within 10 min after AED application, the definitive diagnosis of NCSE was made according to other secondary criteria; ** nystagmoid eye movements, subtle myoclonic jerks; *** ictal-EEG patterns or electroclinical seizures.

Electroclinical criteria	Number of patients
A. EDs > 2.5 Hz	N = 18
1. EEG and clinical improvement after IV AEDs*	4
2. Subtle clinical ictal phenomena during EEG patterns**	8
3. Typical spatiotemporal evolution***	7
B. EDs ≤ 2.5 Hz	N = 17
1. EEG and clinical improvement after IV AEDs*	2
2. Subtle clinical ictal phenomena during EEG patterns**	9
3. Typical spatiotemporal evolution***	13
C. Rhythmic delta/theta activity (>0.5 Hz)	N = 5
1. EEG and clinical improvement after IV AEDs*	1
2. Subtle clinical ictal phenomena during EEG patterns**	1
3. Typical spatiotemporal evolution***	4