Diagnosis of epileptic syndrome after a new onset seizure and its correlation at long-term follow-up: Longitudinal study of 131 patients from the emergency room

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Summary This study aims to demonstrate the reliability of the diagnosis of epilepsy after a new onset seizure, supported by a detailed anamnesis and the complementary tests accessible at the emergency room (ER), such as CT-scan and video-EEG. It was a prospective study including 131 adult patients (55% males, medium age 52.42 ($\pm$21.5)[16—98] years-old, follow-up 25.22 ($\pm$13.69)[12—31] months). In half of cases we could not identify any predisposing factor. Within the first 72 h, patients were included into an epileptic syndrome according to the ILAE 1989 classification, if possible. Thereafter, they were followed-up in the outpatient clinic of the Epilepsy Unit, where seizure recurrence was recorded and further diagnostic examinations were performed. 94.1% of patients initially diagnosed of epilepsy were confirmed as epileptics, and up to 57% of patients could be classified into a particular syndrome from the ER. Conversely, 44.6% of patients with the initial diagnosis of isolated seizure and one third of patients with non-epileptic seizures developed recurrence, switching their initial diagnosis to epilepsy. Both CT-scan and early EEG demonstrated its usefulness evaluating the risk of recurrence after a new onset seizure (Positive predictive value 78% and 88%, respectively). Epileptiform activity was a predictor of seizure recurrence ($p < 0.05$), independently to the moment where the EEG was performed. According to our results, it is realistic to perform the diagnosis of epilepsy after a new onset seizure, although many patients still need further specific examinations, or seizure recurrence, to be diagnosed.
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Introduction

According to the new proposal for epilepsy definition of the International League Against Epilepsy (ILAE), the diagnosis of epilepsy requires the presence of one or more seizures in a patient with an underlying brain disorder which generates predisposition to epileptic seizures, appearing a number of neurobiological, cognitive, psychological and social consequences (Fisher et al., 2005). Therefore, it is affordable to make the diagnosis of epilepsy after a new onset seizure in which semiological and complementary examinations are able to demonstrate a high likelihood of seizure recurrence. Seizures are one of the most frequent causes of neurological pathologies seen in the emergency room (ER). Up to 10% of the global population may experience a seizure throughout their lifetime (Hauser et al., 1996; Hauser and Beghi, 2008). Neurologists often wonder whether a new onset seizure can be the first manifestation of a chronic epileptic condition or a non-epileptic event, such as syncope, TIAs or psychogenic seizures. A second question for physicians is the etiology of seizures, which can be provoked by a direct causal factor in which case the removal of this hypothetical element would prevent the recurrence, or unprovoked seizures with an estimated risk of recurrence about 40% at two years (Hauser and Beghi, 2008; Berg and Shinnar, 1991; Hui et al., 2001; Bora et al., 1995). The proper classification of a single seizure within an epileptic syndrome is relevant to proceed with therapeutics and to establish an early prognosis. Finally, the decision to start a patient on chronic antiepileptic medication (AED) after a new onset seizure is still controversial; since the relation risk—benefit in terms of quality of life has not been clarified yet. Therefore, the diagnosis of epilepsy after a new onset seizure is a challenge for the physician, who must rely on a thorough medical anamnesis to investigate the presence of previous seizures, risk factors and additional evidence from the complementary examinations.

This study aims to demonstrate the reliability of the diagnosis of epilepsy after a new onset seizure, based on proper neurological assessment of the ictal and periictal circumstances and the complementary tests accessible at the ER, such as CT-scan and EEG; and evaluate whether a good correlation exists between the initial epileptic syndrome classification and the final diagnosis at follow-up.

Methods

It was a prospective study that included 131 adult patients who consulted consecutively for a new onset seizure to the ER of our institution, from May 2006 until February 2009. The patients were 55% male and 45% female, the medium age was 52.42 ($\pm$21.5) [16—98] years-old (Table 1). They were examined by a neurologist, and were included if a stereotyped paroxysmal spell highly suggestive of an epileptic seizure was suspected, such as involuntary tonic, clonic, tonic-clonic movements, with or without involvement of consciousness, versive positions, automatisms, sensory auras and characteristic behavioural epileptic disorders. We conducted a detailed medical anamnesis to investigate the presence of relevant familial history, abnormal birth or psychomotor retardation, febrile seizures, cranial trauma, meningitis or encephalitis. We sought to find previous subtle paroxysmal events, as episodes of absences or myoclonus. Patients with previous seizures were excluded. According to the patients or witness outline, we determined the type of

seizure as classified by the ILAE in 1981 (simple partial, complex partial evolving to generalized, generalized or unclassified seizures). We recorded the presence of possible precipitating etiologic factors (febrile syndrome, systemic diseases, ingestion or withdrawal from alcohol or drugs, sleep deprivation, history of stroke, trauma or cranial surgery, etc.). We performed an accurate physical and neurological examination, carrying out biochemical analysis, cell blood count and toxicological screening, and CSF examination if deemed necessary. A CT-scan and a Video-EEG were carried out within 48 h after the admission to the ER. CT-scan was obtained by Siemens (Erlangen, Germany) scanner; using 10 mm slice thickness in cerebral hemispheres and 5 mm slice thickness in the posterior fossa. Axial and coronal orientation was obtained. Iodide intravenous contrast media was used when a tumoral lesion was identified. The CT-scan was considered as pathologic when potential epileptogenic lesions where seen, such as tumors, haemorrhage, ischemic strokes, malformations of cortical development or areas of encephalomalacia. Electroencephalographic, electrocardiographic and thoracic breathing activity recordings were performed with a 16-channel analogical *Nicolet* polygraph and a 32-channel digital *Deltamed* video-electroencephalograph. The EEG was recorded using 0.1—70 Hz band pass. Patients had surface EEG evaluations when scalp silver-chloride electrodes were placed according to the International 10-20 System. Both referential and bipolar montages were used. Recordings lasted for 30 min, and included hyperventilation and photic stimulation at 1—30 Hz. EEG recordings were encoded by two independent electroencephalographists as *abnormal epileptiform* when paroxistic activity such as focal or generalized spikes, polyspikes and sharp waves were seen; *abnormal non-epileptiform*, if focal or generalized slow waves were present; and *normal* if no relevant findings were identified. Within 24 h after all the testing had been performed each patient was presented to a panel of three independent epileptologists, who included them into an epileptic syndrome according to the ILAE 1989 Classification, if possible. Thereafter, the patients were followed-up in the outpatient clinic of the Epilepsy Unit with sequential visits at one, three, six and 12 months after the seizure onset, depending on the patients' characteristics. The visit schedule was changed when unexpected seizures or other medical conditions occurred. Clinical factors such as recurrence were recorded, and further diagnostic examinations were performed during the follow-up when considered necessary. An MRI was done in a 1:5 T scanner (Siemens, Erlangen, Germany), using T1, T2-weighted and FLAIR (fluid-attenuated inversion recovery) images with coronal and axial 5 mm slices. Gadolinium contrast enhancement was done in selected cases. Finally, routine EEGs and sleep-deprived EEGs were recorded in some patients during follow-up.

Descriptive and frequency statistical analyses were obtained and comparisons were performed with SPSS for Windows, version 17.0. Statistical significance for intergroup differences was assessed by Pearson's χ^2 for categorical variables and the Student's t or Mann—Whitney U test for continuous variables. A probability value <0.05 was considered statistically significant.

Results

We enrolled 131 adults with a suspected new onset seizure during the study period (Table 1). The drop out of patients was 10.4% (1.2% were missed and the mortality rate was 9.2%). In the remaining 89.6% patients, the average follow-up was 25.22 ($\pm$13.69) months with a range between 12 and 31 months. Only three patients had a first degree relative affected of epilepsy. Half of the cases presented some presumed related acute or remote etiologic factor, the most frequent being the acute toxic-metabolic cause (20%), followed by intracranial lesions like strokes or tumors (18%) and