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Original article

Underlying neurologic disorders and recurrence rates of status epilepticus in childhood

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Abstract

Background: The underlying neurologic disorders of status epilepticus (SE) in childhood remain poorly characterized. *Methods:* We reviewed 249 consecutive patients with SE, aged 1 month to 18 years, who were referred to Tottori University Hospital from 1984 to 2002. After exclusion of SE patients with acute symptomatic etiology and progressive encephalopathy, such as acute encephalitis/encephalopathy, meningitis, head trauma, or metabolic disorders, we analyzed 112 patients, aged 3 months to 14 years, and focused on the epilepsy classification and perinatal brain damage in these patients. *Results:* Major underlying neurologic disorders were non-symptomatic epilepsy (41 patients, 36.6%), perinatal brain damage (15 patients, 13.4%), non-syndromic mental retardation (17 patients, 15.2%), and congenital disorders including chromosomal abnormalities (13 patients, 11.6%). In non-symptomatic epilepsy, childhood epilepsy with occipital paroxysms (Panayiotopoulos syndrome, 11 patients) and severe myoclonic epilepsy in infancy (SMEI, 6 patients) were common and had high recurrence rates (81.8% and 66.7%, respectively). In patients with a history of perinatal brain damage, preterm birth, neonatal seizure, asphyxia, and neonatal hypoglycemia were frequent. Neonatal hypoglycemia and neonatal seizure were related to the recurrence of SE (100% and 87.5%, respectively). They were mostly diagnosed as symptomatic occipital lobe epilepsy. Parieto-occipital paroxysms were associated with a high recurrence rate of SE (80.6%). *Conclusions:* Although the underlying neurologic disorders of SE are heterogeneous, three specific epileptic syndromes (Panayiotopoulos syndrome, SMEI, and symptomatic occipital lobe epilepsy secondary to neonatal hypoglycemia and neonatal seizure) were the most common causes of SE and were associated with higher recurrence rates.

Keywords: Status epilepticus; Underlying disorders; Recurrence rate; Childhood; Occipital lobe epilepsy; Panayiotopoulos syndrome; SMEI; Mental retardation

1. Introduction

Status epilepticus (SE) is a common pediatric emergency and carries a risk of permanent brain damage or death. In a previous study of over 200 patients with SE seen at Tottori University Hospital in Japan, we found that long seizure duration over two hours and moderate to severe asthmatic attack during SE were associated with neurological sequelae or mortality [1]. Although some epidemiological studies about SE for occurrence rate, age at onset, seizure types, causes, recurrent rate, and prognosis were reported, the underlying neurologic disorders of SE in childhood remain poorly characterized [1–4].

The etiology of SE has usually been classified into five categories; 'acute symptomatic', 'remote symptomatic', 'cryptogenic or idiopathic', 'febrile' and 'progressive encephalopathy' [5]. Although this classification may

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be useful in an epidemiological context, clinically it is more important for pediatricians to know the precise diagnosis of the underlying disorders to predict recurrence of SE. Recurrence rate in each underlying disorder has not been analyzed. For example, anecdotal evidence suggests that patients with severe myoclonic epilepsy in infancy (SMEI) [6] or Panayiotopoulos [7] syndrome are at higher risk of SE, but the incidence in SE patients and recurrence rate have not been determined. The present study aimed to determine the specific neurologic disorders that underlie SE and recurrence rates for SE in each disorder.

2. Methods

2.1 Subjects

A review of the medical records of all infants and children aged 1 month to 18 years who were referred to Tottori University Hospital due to SE from January 1984 to December 2002 identified 249 patients with SE. Patients with acute symptomatic etiology and progressive encephalopathy, such as acute encephalitis/encephalopathy, meningitis, head trauma, or metabolic disorders, were excluded from this study. We also excluded patients with febrile SE from the study of underlying disorders; only recurrence rate was determined in these patients. Finally, 112 patients were enrolled. Underlying neurologic diseases or disorders including epileptic syndrome were determined at last follow-up. For example, a patient who was regarded as having cryptogenic SE at the time of first SE, was diagnosed with epilepsy when unprovoked seizures recurred.

2.2. Study design

Tottori University Hospital serves the western part of Tottori Prefecture and surrounding areas and has an intensive care unit with a 24-h medical care system for pediatric patients. Three local hospitals serve as less intensive patient institutions in this area. SE patients who show no amelioration of symptoms after initial treatment or who have complications are transferred to our hospital. Our hospital also has the only department of child neurology in this region and thus most neurologically ill children, including those with developmental disorders, are referred to our department.

Status epilepticus was defined as any seizure lasting more than 30 min or recurrent seizures lasting a total of more than 30 min without complete recovery of consciousness. Almost all patients received diazepam first. If diazepam failed to control the seizure, phenytoin or thiopental were then administered.

To identify the etiology of SE, routine laboratory examination including a complete blood count, serum liver enzyme, serum glucose, serum calcium, urinalysis, cerebrospinal fluid (CSF), cranial computed tomography or magnetic resonance imaging, and electroencephalogram were performed for each patient, especially at the first SE. For patients with recurrent SE, these analyses were repeated if necessary. Metabolic analyses, including plasma and urine amino acids, urine organic acids, and blood and CSF lactic acid were also performed to identify the cause of SE if required.

The underlying diseases or disorders were determined based on laboratory, physical and neurological findings. Epileptic syndromes were classified according to the International classification of epilepsies, epileptic syndromes and related seizure disorders published in 1989 [8]. Idiopathic and cryptogenic epilepsy were categorized in 'non-symptomatic epilepsy'. Epileptic focus is determined with electroencephalography, radiological findings in cranial computed tomography or magnetic resonance imaging, and seizure semiology. If the EEG focus migrated in the clinical course, the most relevant focus to the seizure was used for the analysis. Patients with mental retardation (MR) in whom the cause or etiology could not be identified and who had no anomalies were classified as 'non-syndromic MR'. In patients with epilepsy, we calculated recurrence rates with respect to epileptic foci (frontal, centro-temporal, parieto-occipital, multifocal, and generalized). In patients with perinatal brain damage, we also looked for possible associations between various factors (neonatal hypoglycemia, neonatal seizure, low birth weight/preterm birth, asphyxia, and intracranial hemorrhage) and recurrence of SE.

3. Results

3.1. Underlying diseases or disorders (Table 1)

The 112 patients consisted of 63 males and 49 females. Age at the onset of SE ranged from 3 months to 14 years (mean 5.2 years). For 9 patients the follow-up period was short (less than 6 months). All of these patients had been previously diagnosed with epilepsy. The other 103 patients were followed up for 6 months to 18 years (mean 4.6 years). No patients died during the follow-up period.

Ninety-seven patients were finally diagnosed with symptomatic or non-symptomatic epilepsy. Forty-one of the 112 patients (36.6%) were diagnosed with non-symptomatic epilepsy, 11 patients of which had early-onset childhood epilepsy with occipital paroxysms (Panayiotopoulos syndrome). Non-syndromic MR was the second most common disorder. Low birth weight/preterm birth, neonatal seizures, asphyxia, and neonatal hypoglycemia were frequent factors in perinatal brain damage and they overlapped in all patients. Many other diseases or disorders were heterogeneous and less frequent.