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Original article

Characteristics of epilepsy occurring in the first four months

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Abstract

Introduction: Epilepsies with an onset during the early infantile period are relatively rare and their characteristics are not well recognized. The aim of this study was to determine the clinical characteristics of epilepsies with an onset during the early infantile period. *Methods:* Clinical information on 73 patients with the onset of epilepsy within the first four months was collected from hospitals affiliated with Nagoya University. Patients were categorized into three groups: the idiopathic (20 patients), cryptogenic (19 patients), and symptomatic groups (34 patients). *Results:* Fourteen (70%) of the 20 patients in the idiopathic group, nine (47%) of the 19 patients in the cryptogenic group, and 10 (29%) of the 34 patients in the symptomatic group had their first seizure within the first month of life. All patients in the idiopathic group, 12 patients (63%) in the cryptogenic group, and 18 patients (53%) in the symptomatic group had partial seizures (PS) alone throughout their clinical course. Four patients in the cryptogenic group and nine in the symptomatic group had PS at the onset, but evolved into spasms later. All patients in the idiopathic group, 13 patients (68%) in the cryptogenic group, and 13 patients (38%) in symptomatic group had experienced no seizures for at least one year at the time of the last follow-up. *Conclusions:* In patients with non-idiopathic epilepsy, an age-dependent evolution of seizure types was often observed. Recognition of this subgroup of patients could be important for the identification of appropriate candidates for early epilepsy surgery.
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Keywords: Epilepsy; Early infantile onset; Seizure; Prognosis

1. Introduction

Researchers are increasingly becoming interested in epilepsy with an early infantile onset, because successful results of epilepsy surgery for pharmaco-resistant epilepsy in early life have been reported [1,2]. Frequent uncontrolled seizures in the early infantile period can

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result in deterioration of cognitive function [3]. Differentiation of surgical candidates from patients who are controllable with antiepileptic medications is important in the early infantile period.

During the neonatal period, some benign or pharmaco-resistant epilepsies are listed as age-specific epileptic syndromes, including benign familial or non-familial neonatal seizures, early myoclonic encephalopathy, and early infantile epileptic encephalopathy (EIEE). Also, many age-specific epileptic syndromes are observed between the ages of 4–5 months and 1 year, including West syndrome, benign partial epilepsy in infancy, and Dravet syndrome [4].

However, the features of epilepsy with an onset during the early infantile period are not well described. In this study, we investigated the age of onset, evolution of seizure types, and prognosis in patients with an onset of epilepsy in the early infantile period to clarify the clinical characteristics of epilepsies in this period.

2. Patients and methods

We investigated the seizure types and prognosis in children who had onset of epilepsy within the first four months after birth and who were referred to seven affiliated hospitals of Nagoya University Graduate School of Medicine between January 1, 1986 and December 31, 2006. Pediatric neurologists at each hospital have reviewed a local database of the hospital and outpatient clinic, and have selected epilepsy patients with onset within 4 months of age during the study period. We excluded patients with acute symptomatic seizures, such as seizures related to hypoxic-ischemic encephalopathy (HIE), intracranial hemorrhage, meningitis, encephalitis, hypocalcaemia, or hypoglycemia. The seven participating facilities (Nagoya University Hospital, Aichi Prefectural Colony Central Hospital, Okazaki City Hospital, Anjo Kosei Hospital, Japanese Red Cross Nagoya First Hospital, Toyota Memorial Hospital, and Aichi Children's Health and Medical Center) include six of the seven certified training institutions and hospitals of the Japanese Society of Child Neurology in Aichi prefecture.

Pediatric neurologists retrospectively reviewed the hospital charts and obtained information on gestational age, birth weight, pre-, peri-, and postnatal histories, the presence or absence of underlying disorders, details of seizure manifestations, EEG findings, neuroimaging studies, including CT and/or MRI, antiepileptic drugs administered and data on their efficacy, and the patient's developmental and seizure outcome. All patients were followed for one year or longer to determine their seizure and developmental outcome. The outcome was evaluated in June 2013. In patients lost to follow-up, the outcome was determined from the clinical records.

Seizure types were determined according to those set out by the Commission on Classification and Terminology of the International League Against Epilepsy (1981, 1989) [5,6]. They were diagnosed using seizure manifestations, interictal EEG recordings, and ictal EEG recordings when they were available and accurate. We focused on evolutional changes in seizure types during the follow-up period for each patient.

Patients were categorized into three groups, based on epilepsy classifications: the idiopathic, cryptogenic, and symptomatic groups. The idiopathic group included patients who had normal developmental outcomes with no known disorder of the brain and had a known idiopathic epileptic syndrome. The cryptogenic group included patients who did not have a known epileptic syndrome, and the etiology was unknown. The symptomatic group included patients who had a known disorder of the brain. We compared seizure types and outcomes among the three groups. Seizure freedom was defined if the patients had had no seizure for at least one year at the time of the last follow-up. We judged motor impairment from the findings of neurological examinations by neurologists in each hospital. We evaluated developmental status using the Wisconsin Intelligence Scale for Children, Tanaka-Binet Intelligence Scale, or Tsumori-Image Developmental Questionnaire. Developmental status was classified as normal when patients had an IQ or DQ score $\geqslant 70$ and as mental impairment when patients had an IQ or DQ score <70 at the final evaluation.

Differences in the age at onset among the three groups were statistically analyzed using the Kruskal–Wallis test. Differences in the number of patients with onset before 1 month of age were also analyzed by Fisher's exact probability test. Differences in seizure and developmental outcome were analyzed by Fisher's exact probability test. Significance was established at $p < 0.05$.

3. Results

Seventy-three infants (32 males) were registered: 20 patients (10 males) were categorized into the idiopathic group; 19 (nine males) into the cryptogenic group; and 34 (13 males) into the symptomatic group. Gestational ages ranged from 34 to 42 (median 39) weeks. Birth weights ranged from 1798 to 4420 (median 3072) g. Ages at last follow-up ranged from 1.3 to 23.4 (median 7.0) years. Table 1 lists the clinical data for the patients in each group. The diagnosed epileptic syndromes in the idiopathic group were benign idiopathic neonatal convulsions (BINC; 10 patients), benign familial neonatal convulsions (BFNC; four patients), and benign infantile convulsions (BIC; six patients). The underlying diseases in the 30 patients in the symptomatic group were remote symptomatic epilepsy of HIE in seven patients, three patients each with hemimegalencephaly, pachygyria,

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