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Original article

A ten-year follow-up cohort study of childhood epilepsy: Changes in epilepsy diagnosis with age

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Abstract

Objective: To elucidate all of the characteristics of childhood epilepsy, we performed a long-term follow-up study on the patients who visited Okayama University Hospital.

Subjects and methods: We retrospectively investigated the patients who were involved in the previous epidemiological study and visited Okayama University Hospital for a period of 10 years after December 31, 1999.

Results: Overall, there were 350 patients' medical records that were evaluated, and 258 patients with complete clinical information available for a 10-year period were enrolled. Ten patients died and the remaining 82 were lost to follow-up. Of 258 patients with complete information, 153 (59.3%) were seizure-free for at least 5 years. One hundred thirty (50.4%) had intellectual disabilities and 77 (29.8%) had motor disabilities, including 75 (29.1%) with both disabilities on December 31, 2009. Thirty-four patients of 350 (9.7%) changed the epilepsy classification during follow-up. With regard to ten patients who died, nine of them had symptomatic epilepsy, particularly those with severe underlying disorders with an onset during the first year of life.

Conclusion: Clinical status considerably changed during the decade-long follow-up period in childhood epilepsy. Changes in the epilepsy diagnosis are especially important and should be taken into account in the long-term care of children with epilepsy.

Keywords: Epilepsy; Clinical course; Longitudinal study; Childhood

1. Introduction

To determine all of the characteristics of childhood epilepsy, it is important to investigate its epidemiology not only on a single prevalence day but also the detailed clinical course of the affected patients over a long period after the prevalence day, because epilepsy is chronic and includes heterogeneous disorders with variable outcomes. Epidemiological studies of childhood epilepsy have been undertaken in various countries [1–7]. However, there have been few such studies with long-term follow-up for childhood epilepsy in Japan [8]. Most of the published long-term follow-up epidemiological studies assessed outcomes in terms of remission or death [8–13], and there are only a few studies on the course of epilepsy including changes in classification [14,15].

It is possible that diagnosis of epilepsy classification may be changed because of age-dependent changes and/or identification of previously unknown etiology through advances in neuroimaging and genetic examination. Thus, we aimed to clarify the long-term course of

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childhood epilepsy in Japan from an epidemiological perspective. Oka et al. performed a large-scale population-based survey of childhood epilepsy in Okayama Prefecture, Japan using the prevalence day of December 31, 1999 [7]. Based on this study, we followed patients who had visited Okayama University Hospital for a period of 10 years. We aimed to disclose the decade-long burdens of childhood epilepsy on the patients, their family and society in this study.

2. Subjects and methods

2.1. Patients

Our previous neuroepidemiological survey of childhood epilepsy was based on all children aged <13 years living in Okayama Prefecture, Japan [7]. The prevalence day was December 31, 1999. The prevalence rate and distribution of epilepsy and epileptic syndromes were reported according to the classification by the International League Against Epilepsy (ILAE) in 1989 [16]. In this previous study, we determined that the patients who had taken antiepileptic drugs (AEDs) and/or who had experienced at least one seizure during the last five years had active epilepsy. Of the 2220 identified patients with active epilepsy, 510 (289 males, 221 females) had visited the Department of Child Neurology at Okayama University Hospital at least once, and clinical information was available after the prevalence day for 350 patients. Out of the 350 patients, 82 were lost to follow-up during the 10-year period after December 31,1999. In the present study, we performed a follow-up investigation of the remaining 268 patients (composed of Group 1, which contained 258 live patients, and Group 2, which contained 10 who died during follow–up) to clarify their detailed, clinical course of epilepsy, seizure outcomes, and disability. We used the same definition of active epilepsy as the previous study for consistency. Similarly, we also used the same ILAE 1989 classification [16], but new diagnostic entities such as Panayiotopoulos syndrome (PS) were included according to Berg et al. [17]. This study was approved by the Okayama University Ethics Committee with the following stipulation: investigation of patients who visited the Okayama University Hospital was approved but that of patients who did not visit this hospital was not permitted as a condition of ethics approval for the initial study.

2.2. Statistical analysis

We performed the Wilcoxon signed-rank test to compare the frequency of seizures and the number of AEDs between 1999 and 2009. The frequency of seizures (no seizure $\geqslant$5 years, no seizure for >1 year and <5 years, yearly, monthly, weekly, daily) was ranked as indices 1 through 6, and the number of AEDs (zero, one, two, three, four or more) as indices 1 through 4 (Table 4). We used SPSS Statistics (Japanese ver. 23; IBM Japan, Ltd., Tokyo, Japan) for this analysis.

3. Results

3.1. Group 1 patients

Distribution of the epilepsy classification in the 258 patients in 1999 and 2009 is shown in Table 1 and Supplementary Fig. 1: 163 and 163, respectively, were diagnosed with localization-related epilepsy, 72 and 68, respectively, with generalized epilepsy, and 14 and 19, respectively, with epilepsies undetermined (either focal or generalized). Sufficient information to make an epilepsy classification was not available for nine and eight patients, respectively.

With respect to the age distribution pattern, five (1.9%) patients were under one year of age, 55 (21.3%) were 1–4 years old, 124 (48.1%) were 5–9 years old, and 74 (28.7%) were 10–12 years old in 1999.

The mean age of the 258 patients was 7 years 7 months (range, 3 months–12 years 11 months) on December 31, 1999. The mean age at onset of epilepsy was exactly 3 years (range, 0 months–11 years 10 months), and 87 patients (33.7%) had an initial seizure during the first year of life.

Patients' underlying diseases are listed in Table 2 and include perinatal complications, cerebral dysgenesis/tumor, neurocutaneous syndromes, cerebrovascular disorder, genetic neurologic disease, sequelae of the central nervous system infection and hypoxic-ischemic encephalopathy. Etiologies were newly identified during follow-up in nine patients including focal cortical dysplasia (FCD) in three, *SCN1A* mutations in three, hippocampal sclerosis in two, and dysembryoplastic neuroepithelial tumor (DNT) in one. In addition, hippocampal sclerosis developed after encephalitis during follow-up in one patient. On December 31, 2009, no underlying diseases were found in the remaining 159 (61.6%) patients including 54 (20.9%) with only a family history of genetic factors for epilepsy or febrile seizures.

Diagnosis of epilepsy classification was changed during follow-up in 26 patients as shown in Table 3. One patient diagnosed with idiopathic localization-related epilepsy (ILRE; childhood epilepsy with occipital paroxysms) on the prevalence day was re-diagnosed with PS by 2009. Of 82 patients diagnosed with symptomatic localization-related epilepsy (SLRE) on the prevalence day, two showed evolution to different types of epilepsy (one to Lennox-Gastaut syndrome [LGS] and the other to epilepsy with continuous spike-waves during slow-wave sleep [ECSWS]). Another patient who, from infancy, had seizures that were often associated with fever but was still in the early phase of the disease on