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Comparative study of typical and atypical benign epilepsy with centrotemporal spikes (Rolandic epilepsy)

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= Abstract =

Purpose : This study aims to examine and compare the features of rolandic epilepsy.
Methods : Of 158 patients selected retrospectively, 116 had typical (group A) and 42 had atypical (group B) rolandic epilepsy, as defined by Worrall's criteria.
Results : The age at onset of the seizures in group A was 8.6±2.0 y and 6.2±1.7 y in group B ($P>0.05$). Among the 40 patients who underwent neuroimaging studies (25 patients in group A and 15 patients in group B), abnormal findings in group B included ventricular dilatation, mild cortical atrophy, and partial agenesis of corpus callosum. group A had no abnormal findings. The frequency of seizures was 2.0±1.0 and 2.3±1.2 per month in groups A and B respectively. Seizure control from the initial anticonvulsant treatment was achieved within 3 months in group A, and 3 to 12 months in group B. A 2-year remission rate was noted in 105 patients in group A and in 38 patients in group B. Of these, the recurrence rate after 2 y was 13 in group A and 12 in group B.
Conclusion : Age of onset of seizures, gender, frequency of seizures before therapy, and 2-y remission rate were not significantly different in the 2 groups. However, neuroimaging abnormalities, the time to achieving seizure control from the initial anticonvulsant treatment, and the recurrence rate after being seizure-free for 2 y were significantly different in the 2 groups. **(Korean J Pediatr 2008;51:1085-1089)**

Key Words : Benign epilepsy with centrotemporal spikes (BECT), Typical benign rolandic epilepsy, Atypical benign rolandic epilepsy, Worralls criteria

Introduction

Benign epilepsy with centrotemporal spikes (BECT), also called benign rolandic epilepsy, is the most common partial epilepsy syndrome in the pediatric age group, accounting for 15-24% of pediatric patients with epilepsy[1]. The peak age of onset for this type of epilepsy is reported to be 9 years of age, with complete resolution after 16 years of age[2]. BECT is a sleep-related disorder. Classically, BECT occurs during sleep, usually shortly after falling asleep or before awakening. The seizure often begins focally with clonic movements of the mouth, guttural sounds, increased salivation, and a strange sensation of the tongue; it may become secondarily generalized. The typical electroencephalogram (EEG) pattern shows high-voltage spikes or spike and waves in the centrotemporal area of the brain with a normal background[3, 4]. Neuroimaging studies are usually normal. Patients with this form of epilepsy have an excellent prognosis with no developmental impairments or neurological deficits[1, 2]. Although BECT is easily recognized by its characteristic features, atypical clinical and EEG features have been reported to be common. The atypical features were defined as suggested by Wirrel's criteria[5]. They proposed that the atypical clinical features included diurnal seizures, aura and screaming as features of the seizure and postictal Todd's paralysis, the EEG features included unusual locations, atypical spike morphology and abnormal background activity. However, there are no comparative studies comparing the features of typical and atypical BECT. Therefore the aim of this study was to compare the clinical course and the features of children with the typical form of BECT with those who have the atypical form. An understanding of the clinical course and patient characteristics of the atypical form may improve our understanding of the natural history of this disorder as well as patient management and prognosis.

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Materials and Methods

One hundred and fifty eight children with benign rolandic epilepsy were included from the department of pediatrics at Kyunghee University Hospital between January 1, 2002 and December 31, 2006. Patients with the Landau-Kleffner syndrome and continuous spikes and waves during slow-wave sleep (CSWS) were excluded from the study. We retrospectively reviewed demographic data (age of onset and gender), neuroimaging studies, seizure frequency prior to therapy, time to achieving seizure control after the initial treatment with anticonvulsant drugs, two year remission rate, and recurrence after 2 years of being seizure free. Based on the clinical features, the patients were subdivided into two groups : group A consisted of children with the typical form of benign rolandic epilepsy and group B of children with the atypical form. group A included 116 children who met the classic criteria for BECT and group B had 42 children who did not fulfill the classical criteria. The atypical features were defined as suggested by Wirrel's criteria[5] and included diurnal seizures, aura and screaming as features of the seizure and postictal Todd's paralysis. The t test and the chi-square test were used to compare the data from the two groups. Statistical significance was set at a $P<0.05$.

Results

1. Age at onset of the seizures

The age at onset of the seizures in group A was 8.6±2.0 years old and it was 6.2±1.7 in group B. The seizures started younger in group B than in group A; however, the difference was not statistically significant ($P>0.05$).

2. Gender

Among the 158 patients, 96 patients (60.8%) were males and 62 patients (39.2%) were females. The ratio of males to females was 1.6:1. Among the 42 patients with atypical rolandic epilepsy, 24 were males and 18 were females. Within group B there were more males (24/42; 57.1%) than females (18/42; 42.9%). The ratio of males to females in group B (male: 24, female: 18) was 1.3:1. The number of males and females were not significantly different in comparisons between the two groups ($P>0.05$).

3. Neuroimaging studies

Among the 158 patients, 40 patients had neuroimaging studies (25 patients in group A, 15 patients in group B). Among the 40 patients with neuroimaging records, 30 had normal findings and 10 had abnormal findings. All 25 patients in group A had normal neuroimaging findings, but 10 patients in group B had abnormal neuroimaging results. The abnormal neuroimaging findings included ventricular dilatation (4 patients), mild cortical atrophy (4 patients), and partial agenesis of corpus callosum (2 patients). The difference between group A and group B were significant ($P<0.05$).

4. Frequency of seizures prior to therapy

The frequency of seizures attack prior to treatment with anticonvulsant drugs was 2.0±1.0 per month in group A and 2.3±1.2 per month in group B. This difference was not statistically significant ($P>0.05$).

5. Time to seizure control

The time to seizure control from the initial treatment with anticonvulsant drugs to control of the seizures was within 3 months in group A and 3 to 12 months in group B. The difference between the two groups was statistically significant ($P<0.05$).

6. Two year remission rate

A two year remission rate was observed in 105 out of 116 patients (90.5%) in group A and in 38 out of 42 patients (90.4 %) in group B. This difference was not statistically significant ($P>0.05$).

7. The recurrence rate after being seizure free for two years

The recurrence rate after being seizure free for two years was 13 out of 105 patients (12.4%) in group A and 12 out of 32 patients (37.5%) in group B. This difference was statistically significant in comparisons between the two groups ($P<0.05$).

The clinical and seizure characteristics of the patients with the typical form of BECT as well as the atypical form are shown in Table 1.

Discussion

Martinus Rulandus described the first case of BECT in the

Table 1. The Clinical and Seizure Characteristics of Patients with the Typical form of benign Epilepsy with Centrotemporal Spikes (rolandic epilepsy) and the Atypical Form (n=158)

	Group A	Group B
Number of patients	116	42
Male/Female	72/44	24/18
Age at onset of seizures (years)	8.6±2.0	6.2±1.7
Neuroimaging study	25/158	15/58
Abnormal finding	0/25	10/15 Ventricular dilatation (4) Mild cortical atrophy (4) Partial agenesis of corpus callosum (2)
Seizure frequency prior to therapy (per month)	2.0±1.0	2.3±1.2
Duration of seizure control from initial anticonvulsant drugs administration	within 3 month	within 3 to 10 months
Two years remission rate	105/116 (90.5%)	38/42 (90.4%)
Recurrence after 2 years seizure free period	13/105 (12.4%)	12/32 (37.5%)

Group A : Typical form of BECT, Group B : Atypical form of BECT

16th century[6]. Nayrac and Beaussart described the clinical features of BECT in 1958[7]. BECT is the most common childhood partial epilepsy syndrome[1]. BECT is characterized by consistent features including the age of onset, pattern of the seizures, neurodevelopmental profile, neuroimaging, and EEG findings. BECT usually begins between 3 and 13 years of age with a peak at 9 and completely disappears after 16 years of age[8]. Genetic factors likely play a signigicant role in BECT. However, the genes responsible for BECT has not yet been identified. In the studies reported by Bray and Wiser[9] and Heijbel et al.[10] centrotemporal sharp waves were reported to be inherited as an autosomal dominant trait with age-specific expression. However, only a small percentage of the children with centrotmporal sharp waves develops clinical seizures. It seems that whether a child develops seizures depends on a variety of other inherited factors. These other factors may be polygenic. Doose and Baier[11] proposed that BECT has a multifactorial pathogenesis and a diverse phenotype. Therefore, currently it is thought that BECT is likely a multifactorial disorder rather than a disorder related to a single gene abnormality[12].

The seizures associated with BECT involve the area around the lower portion of the central gyrus of Rolando. By stimulating this area, symptoms of BECT are produced13). Classically, BECT occurs during sleep, usually shortly after falling asleep or before awakening[12]. The seizure begins focally with clonic movements of the mouth, guttural sounds, increased salivation, and a strange sensation of the tongue; it may become secondarily generalized[14]. Because the seizures occur during sleep, the focal components of the seizures may be missed. The EEG patterns show characteristic high-voltage spikes or spike and waves situated unilaterally or bilaterally in the centrotemporal area that may shift from side to side with a normal background. The seizures generally stop by middle adolescence.

The typical forms of BECT are easily recognized due to their characteristic features. However, there are many reported atypical forms of BECT. Wirrel et al[5]. proposed that the atypical clinical features included status epilepticus, developmental delay, daytime-only seizures, screaming as a seizure component, and postictal Todd's palsy, the EEG features included unusual locations, atypical spike morphology and abnormal background activity. In a study reported by Wirrell et al.[5], atypical clinical features were seen in 50% of patients with BECT and atypical EEG features in 31% of patients with BECT. Therefore, a comparison of the clinical course and outcome of children with the typical form of BECT and those with the atypical form is needed to improve our understanding of the natural history of these clinical findings.

In our study, the children in group B had an earlier age at the onset of their seizures: 6.2±1.7 years compared to 8.6 ±2.0 in group A. However, this difference was not statistically significant ($P>0.05$). This is consistent with other studies that have found no difference in age at the onset of the seizures[15, 16]. However, there are other studies that have reported an earlier age of the onset of the seizures in children with the atypical form of BECT, especially those with frequent seizure recurrence, medical refractoriness, and cognitive dysfunction[17, 18]. Forty patients in our study had neuroimaging studies (25 patients in group A and 15 patients in group B). Among the 40 patients with neuroimaging re-

cords, 30 had normal and 10 had abnormal findings. The abnormal neuroimaging findings included ventricular dilation (4 patients), mild cortical atrophy (4 patients), and partial agenesis of corpus callosum (2 patients), in group B patients; however group A patients had no abnormal neuroimaging findings ($P<0.05$). Neuroimaging for patients with typical benign rolandic epilepsy is generally not indicated. Although abnormal neuroimaging findings were only found with the atypical form of BECT in our study, the spectrum of atypical features in BECT has not yet been delineated and definitive guidelines for neuroimaging are not yet available.

In cases with infrequent, nocturnal, partial seizures, it is generally accepted that anticonvulsant treatment can be withheld. If recurrent generalized or diurnal seizures occur or if the seizures are disturbing the children and their parents, treatment with anticonvulsant drugs is usually started[12]. The frequency of seizures prior to therapy was 2.0±1.0 per month in group A and 2.3±1.2 per month in group B; the difference was not statistically significant ($P>0.05$). The two year remission rate was 105 out of 116 patients (90.5%) in group A and 38 out of 42 patients (90.4%) in group B; this difference was not statistically significant ($P>0.05$). Both groups were seizure free by two years after the onset of seizures. These findings suggest that the presence or absence of atypical features does not appear to influence the response to anticonvulsant treatment[5].

Classically, the long-term prognosis for BECT is excellent with almost all patients achieving complete remission without any neurological deficits by the adolescence[1, 2]. To determine patient outcome, the two-year remission rate, the duration of seizure control and the recurrence rate were used as the study variables in this investigation. The time to achieving seizure control from the initial anticonvulsant treatment administration to seizure control was reached within 3 months in group A, and 3 to 12 months in group B; the difference between the two groups was statistically significant ($P<0.05$). The recurrence rate after a 2 year seizure free period was 13 out of 105 patients (12.4%) in group A and 12 out of 32 patients (37.5%) in group B; the difference between the two groups was statistically significant ($P<0.05$). The duration of seizure control was longer and the recurrence rate higher in group B patients. In a prior study reported by Verrotti et al.[19], the authors suggested that for children with the atypical form of BECT, although the response to anticonvulsant treatment and the frequency of seizures are similar to the typical form, the long-term outcome is frequently associated with behavioral problems and learning disabilities. In addition, Yung et al.[20] showed that 31% of children with BECT manifested cognitive and behavioral problems. Among these patients, those children with atypical features of BECT had a much higher incidence of behavioral and developmental problems. Furthermore, Datta et al.[14] reported that nearly twice the number of children with the atypical form of BECT, compared to the typical form, were on more than one anticonvulsant drug, due to incomplete seizure control. These results suggest that children with the atypical form of BECT may have an increased frequency of seizures that are more difficult to control when compared to the seizures of children with the typical form. However, they suggested that seizure control and the long-term outcome are similar in the typical and atypical forms of BECT, although the atypical form may be more difficult to control and patients with atypical features have a much higher incidence of behavioral comorbidities.

It has been reported that the atypical form of BECT is common. An understanding of the clinical course and features of the atypical form may help with the management of patients and better understanding of the prognosis of this disorder. Therefore, we compared the clinical course and features of children with the typical form of BECT with those of children with the atypical form. However, the long-term outcome including behavioral problems and learning disabilities was not determined in this study. Therefore a comparative long-term study investigating the outcome in children with typical and atypical forms of BECT is need to improve our understanding of the natural history of this disorder, patient management and prognosis.

한 글 요 약

중심 측두부 극파를 보이는 전형적 및 비전형적 양성 부분 간진의 비교 연구

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목 적 : 비전형적 롤란도 간질이 드물지 않게 있지만, 전형적 및 비전형적 롤란도 간질의 비교 연구가 거의 없는 상태이다. 본 연구는 전형적 및 비전형적 롤란도 간질의 임상 특징을 알아보고 비교하기 위하여 시행하였다.

방 법 : 2002년 1월 1일부터 2006년 12월 31일까지 경희의료원을 내원한 롤란도 간질 환자 158명을 선별하여 임상 증상, 경과, 관해율, 재발 등을 후향적으로 연구 하였다. Wirrel 기준으로 116

명의 전형적 롤란도 간질군(A군)과 42명의 비전형적 롤란도 간질군(B군)으로 분류하였다.

결 과 : 1) 경련 시작 나이 : A군은 8.6±1.7세, B군은 6.2±1.7세에 경련을 시작하였다. B군이 A군보다 더 일찍 경련이 시작하였지만 통계적 유의성은 없었다(P<0.05). 2) 성별 : 총 158명의 환자 중, 남자가 96명, 여자가 62명 이였다. 남녀 비는 1.6:1 이였다. 42명의 비전형적 롤란도 간질환자(B군) 중, 24명이 남자, 18명이 여자였고, 남녀 비는 1.3:1 이였다. 통계적 유의성은 없었다(P>0.05). 3) 40명의 환자에서 뇌 영상 촬영을 하였다(A군 25명, B군 15명). B군 뇌 영상에서 뇌실 확장(4명), 경증 겉질 위축(4명), 뇌량의 부분적 무발생(2명) 등의 이상 소견이 발견 되었다. A군은 뇌 영상에서 이상이 없었다(P<0.05). 4) 치료 시작 전 경련의 빈도 : A군은 한 달에 2.0±1.0회의 경련을 보였고, B군은 한 달에 2.3±1.2회의 경련을 보였다. 두 군간 통계적 유의성은 없었다(P>0.05). 5) 처음 항경련제 투여 후 경련을 조절하는데 걸린 기간 : A군은 3개월 내, B군은 3-12개월에 조절되었다(P<0.05). 6) 2년간 경련을 보이지 않는 관해율 : A군 116명 환자 중 105명이 관해를 보였고(90.5%), B군 42명 환자 중 38명이 관해를 보였다(90.4%)(P>0.05). 7) 2년간 경련이 없는 관해를 보인 후의 재발률 : A군은 105명의 환자 중 13명이 재발하였고(12.4%), B군은 32명의 환자 중 12명이 재발하였다(37.5%)(P<0.05).

결 론 : 이번 연구에서는 비전형적 롤란딕 간질 환자군(B군)의 경련이 더 일찍 시작 되었으나 유의한 통계적 차이는 없었다. 성별, 치료 시작 전 경련의 빈도, 2년간 경련을 보이지 않는 관해율 등은 두 군간 차이가 없었다. 그러나 뇌 영상 촬영에서의 이상 소견, 처음 항경련제 투여 후 경련 조절 기간, 2년간 경련을 보이지 않는 관해 후의 재발률 등은 두 군간 유의한 통계적 차이가 있었다.

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