Evaluation of Behavior and Cognitive Function in Children with Myoclonic Astatic Epilepsy

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Abstract

Background: Myoclonic astatic epilepsy (MAE) is an idiopathic and generalized childhood epileptic syndrome. Although several studies have reported on cognitive function and intellectual outcome in MAE, little is known about the behavioral problems associated with this disease. The aim of this study was to clarify behavior and cognitive function in children with MAE.

Methods: Four children who were diagnosed as having MAE using the proposed criteria of the International Classification of Epilepsies were retrospectively analyzed using patient records with regard to clinical and neuropsychological findings such as age of seizure onset, semiology and severity of seizures, treatment course, behavioral problems, EEG findings, and WISC-III and Pervasive Developmental Disorders Autism Society Japan Rating Scale (PARS) scores that indicate the tendency of autistic behaviors.

Results: Disease onset in our cohort ranged from 9 to 35 months of age. Seizures were controlled within 3-8 months over a follow-up period of 4-12 years. All patients had borderline normal intelligence (mean IQ: 75.8 at 5-7 years of age) and exhibited impaired coordination, clumsiness, hyperactivity or impulsivity, and impaired social interaction after improvement of seizures. Though these autistic social problems manifested gradually, the children were able to adapt to school life with appropriate support. Interestingly, the behaviors of impaired social interaction and hyperactivity or impulsivity had already been observed before the onset of MAE in most patients, whose PARS scores were all higher than reference values (<9) during infancy.

Conclusion: Our results showed that children with MAE tend to have autistic behavioral problems and mild intellectual impairment along with wide ranges in WISC-III subtest scores. These behavioral and cognitive features appear to exist before the onset of epilepsy.

Keywords: Myoclonic astatic epilepsy; Doose syndrome; Cognitive function; Behavior; Autism spectrum disorders

Introduction

Myoclonic astatic epilepsy (MAE) is an idiopathic, generalized form of childhood epilepsy. As initially described by Doose in 1970, this disease is characterized by different seizure types, generalized spike and wave discharges, and slow waves or slowing down of background activity in electroencephalogram (EEG) [1]. MAE occurs in children with previously normal psychomotor development. With regard to cognitive function and intelligence outcome, 26-80% of MAE patients were reported to be intellectually normal, with others having mildly to moderately impaired intelligence [1-4]. However, little is known about the behavioral problems in MAE and the relationships between the symptoms of epilepsy, cognitive function, and behavior. The aim of this study was to clarify these features in children with MAE.

Methods

We enrolled 4 children with MAE who had been referred to the pediatric department of Shinshu University Hospital between 2003 and 2008, and who satisfied the following criteria; 1) normal development before the onset of epilepsy and the absence of organic cerebral abnormalities, 2) onset of myoclonic, myoclonic-astatic, or astatic seizures between 7 months and 6 years of age, 3) presence of generalized spike- or polyspike-wave EEG discharges at 2-3 c/s without focal spike discharges, 4) follow-up for more than 3 years, 5) exclusion of severe and benign myoclonic epilepsy in infants and cryptogenic Lennox-Gastaut syndrome based on International League Against Epilepsy (ILAE) definitions [5]. We retrospectively analyzed patient records with regard to clinical and neuropsychological findings that included age of seizure onset, semiology and severity of seizures, treatment course, behavioral problems, EEG findings, and Wechsler Intelligence Scale for Children-third edition (WISC-III) and Pervasive Developmental Disorders Autism Society Japan Rating Scale (PARS) scores that indicated the tendency of autistic behaviors. Informed consent was obtained from all parents.

Results

Patient

Representative patient 1 is the second child of twins of healthy non-consanguineous parents. The boy was delivered at 35 weeks of gestation by Caesarian section (Table 1). His birth weight was 1111 grams. He experienced transient neonatal pulmonary hypertension and cardiac failure that was treated without any obvious ensuing neurological impairments. There was a family history of epilepsy. His growth and development before the onset of epilepsy were all higher than reference values (<9) during infancy.

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Conflict of Interest

The authors have no conflicts of interest to declare.

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Developmental course were normal. After an initial tonic seizure that lasted for 1 minute at the age of 2 years and 11 months, several types of seizures, including atonic, myoclonic, and absence seizures, were observed and increased to up to 400 times per day. Interictal EEG showed diffuse spike and wave or polyspike and wave discharges. Ictal records indicated diffuse spike and wave complexes and 2.5 c/s spike and wave bursts corresponding to atonic seizures and absence attacks, respectively. Blood, cerebrospinal fluid, and MRI findings were all normal. MAE was diagnosed and the patient was treated with valproate, lamotrigine, ethosuximide (PHT), and clobazam (CLB) in turn, before establishing a course of combined therapy with PHT, ESM, and CLB for seizure control.

Concerning psychosocial development, the patient had already exhibited mild autistic behaviors, such as a lack of interest in people, restricted interest in play, and resistance to changes, before the onset of MAE through longitudinal observations made also before the onset of MAE through longitudinal observations made in our cohort, all children had borderline intellectual impairment and impaired social interaction were witnessed for all children. Patient 2 was noted to have lessened hyperactivity or impulsivity at the age of 11. Restricted interests or inflexibility was seen in 3 out of 4 patients. Though these autistic social problems manifested gradually, the children were able to adapt to normal school life. PARS scores were higher than reference values (<9) in all 4 patients during infancy. Regarding cognitive function, the patients were evaluated by WISC-III at an age of 5-7 years. All had borderline normal intelligence. Although the highest and lowest WISC-III subtest scores for each child varied greatly, no discernible tendencies were evident.

**Results of 4 patients**

After excluding 1 patient due to a short follow-up period, 4 subjects were enrolled in this study. The clinical characteristics of our cohort are summarized in Table 1. The age of MAE onset was 9-35 months old. All patients achieved complete control of seizures within 3-8 months during an observation period of 4-12 years after seizure onset.

The neuropsychological features of our cohort are presented in Table 2. All patients had normal or slight retardation of motor and language development, and all were noted to have impaired social interaction before the onset of MAE. Hyperactivity or impulsivity was also observed in the group before disease onset except for patient 4, who was too young to evaluate. No patient showed developmental regression despite frequent seizures. After achieving seizure control, impaired coordination, clumsiness, hyperactivity or impulsivity, and impaired social interaction were witnessed for all children. Patient 2 was noted to have lessened hyperactivity or impulsivity at the age of 11. Restricted interests or inflexibility was seen in 3 out of 4 patients. Though these autistic social problems manifested gradually, the children were able to adapt to normal school life. PARS scores were higher than reference values (<9) in all 4 patients during infancy. Regarding cognitive function, the patients were evaluated by WISC-III at an age of 5-7 years. All had borderline normal intelligence. Although the highest and lowest WISC-III subtest scores for each child varied greatly, no discernible tendencies were evident.

**Discussion**

All 4 cases met the diagnostic criteria for autism spectrum disorders (ASD), but not for typical Kanner type autism or Asperger's syndrome. Accordingly, the patients exhibited impaired social interaction and sympathy for other people and had inflexibility and a restricted range of interests. As they rarely asserted themselves strongly or attacked others, all children could adapt to school life with appropriate support. There have been earlier reports of behavioral problems in patients with MAE describing withdrawn, depressed, or aggressive behavior [4], impulsivity and distractibility [6], attention problems [4,7], and hyperkinesia [7]. These studies also indicated that some MAE patients might display behaviors consistent with ASD. We found that all of our patients showed age-dependent autistic behaviors not only after, but also before the onset of MAE through longitudinal observations made using detailed developmental histories.

Several past studies on cognitive function in MAE described incidences of intellectual impairment, with normal level intelligence present in 26% [1], 59% [2], and 80% [3] of subjects. Trivisano et al. suggested that cognitive prognosis was related to genetic factors rather than seizure semiology or time until seizure control in a prospective observation of 18 MAE children [4]. Another report showed poor cognitive prognosis to be associated with tonic or intractable seizures [8]. Although there were no common tendencies among cognitive profiles in our cohort, all children had borderline intellectual impairment and a wide range of WISC-III subtest scores. To our knowledge, there has been no report describing the differences in cognitive profiles among

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**Table 1: Clinical characteristics of patients.**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age at onset (mo.)</th>
<th>Seizure type</th>
<th>Seizure frequency</th>
<th>Age at remission (mo.)</th>
<th>Epilepsy duration (mo.)</th>
<th>Febrile convulsion</th>
<th>Family history of epilepsy</th>
<th>EEG findings</th>
<th>Treatment</th>
<th>Effective drug(s)</th>
<th>Follow-up period (years)</th>
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<td>43</td>
<td>8</td>
<td>+</td>
<td>+</td>
<td>SBA</td>
<td>VPA, ESM, ZNS, CLB, PHT</td>
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<td>2</td>
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<tr>
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<td>M, DA, T</td>
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<td>3</td>
<td>+</td>
<td>+</td>
<td>SBA</td>
<td>VPA, ESM, ZNS, CLB, PHT</td>
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<td>12</td>
<td>3</td>
</tr>
<tr>
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<td>42</td>
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<td>+</td>
<td>+</td>
<td>SBA</td>
<td>VPA, ESM, ZNS, CLB, PHT</td>
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<td>4</td>
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<tr>
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<td>9</td>
<td>M, DA</td>
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<td>3</td>
<td>+</td>
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<td>SBA</td>
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<td>VPA, ESM, ZNS, CLB, PHT</td>
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<td>5</td>
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</tbody>
</table>
before onset

patient 1 | patient 2 | patient 3 | patient 4
--- | --- | --- | ---
motor retardation | ± | ± | - | ±
language delay | - | ± | - | -
hyperactivity or impulsivity | + | + | + | -
restricted interests or inflexibility | + | + | - | -
impaired social interaction | + | + | + | -

after seizure remission

patient 1 | patient 2 | patient 3 | patient 4
--- | --- | --- | ---
motor coordination deficits | + | + | + | +
difficulty with verbal communication | - | + | + | -
hyperactivity or impulsivity | + | + | + | -
restricted interests or inflexibility | + | + | - | -
impaired social interaction | + | + | + | -

PARS score | 13 | 11 | 9 | 17

WISC-III scores

<table>
<thead>
<tr>
<th>age at evaluation</th>
<th>WISC-III</th>
<th>WISC-IV</th>
</tr>
</thead>
<tbody>
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<td>84</td>
</tr>
<tr>
<td>10Y</td>
<td>84</td>
<td>94</td>
</tr>
<tr>
<td>12Y</td>
<td>94</td>
<td>99</td>
</tr>
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</table>

WISC-III, Wechsler Intelligence Scale for Children - third edition; WISC-IV, Wechsler Intelligence Scale for Children - fourth edition; VIQ, verbal intelligence quotient; PIQ, performance intelligence quotient; FIQ, full scale intelligence quotient; VCI, verbal comprehension index; POI, perceptual reasoning index; FDI, freedom from distractibility index; PSI, processing speed index

Table 2: Neuropsychological features of patients.

Table 3: Intelligence scales for patient 1

individuals with MAE to date. Cognitive profiles do not generally reveal common tendencies in people with ASD, but WISC-III subtest score ranges tend to be large in such individuals, which is consistent with our results. Although we observed autistic behavioral problems before MAE onset, it was impossible to precisely analyze cognitive function before the start of seizures because of our group's age. On the other hand, a recent study showed that patients with juvenile myoclonic epilepsy had cognitive impairment due to frontal lobe dysfunction that had presented before the onset of epilepsy. These findings suggest that both autistic behavior and impaired cognitive function in MAE patients might exist before seizure onset. Therefore, close observation and evaluation of behavior and cognition in patients with MAE are recommended, even during infancy.

Conclusions

Patients with MAE tend to have autistic behavioral problems, mild intellectual impairment, and large variability among WISC-III subtest scores. Behavioral, and possibly cognition, features are considered to be present before the onset of epilepsy.

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References


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