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Clinical Characteristics of Children with Mental Retardation of Unknown Etiology in Korea

The purpose of this study was to investigate the clinical characteristics of children with mental retardation (MR) of unknown etiology for early recognition and intervention. In this study, we defined children with MR of unknown etiology as those without clear etiologies for MR despite extensive evaluation and were not associated with pathological behavioral problems such as pervasive developmental disorders and attention-deficit/hyperactivity disorder. The clinical characteristics of children with MR of unknown etiology were as follows. 1) MR of unknown etiology was 48.8% of all MR. 2) MR of unknown etiology was more common in males. 3) Delayed language development was a leading factor that made the parents of children with MR of unknown etiology seek help from physicians. However, most of the children with MR of unknown etiology showed a relatively uniform delay in several areas of development. 4) Most children with MR of unknown etiology were delayed walkers. 5) Most children with MR of unknown etiology were mild cases.

Key Words : *Mental retardation*

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INTRODUCTION

Mental retardation (MR) is one of the most common disabilities in children and the prevalence rate of MR is known to be approximately 3% of children of school age (1). Recent report from the Republic of China revealed that intellectual disability accounts for 66% of all handicapped children, making it the most frequent childhood disability (2).

Brain dysfunction is a basis for MR (3). In one study, 40% of the children with MR had a genetic explanation for their MR, 20% of them had an environmental cause, and the remainder could not be classified (4). Generally, the cause of MR is unknown in approximately 30% of cases in severe MR and in about 50% of cases in mild MR despite extensive evaluations, while in about 50% of the MR cases, they had more than one cause (1, 5, 6).

Early diagnosis and rehabilitation for children with MR are indispensable for their social integration and economically productive life in the future (1, 2). However, our clinical impression is that a medical diagnosis, rehabilitation and educational services tend to be more delayed for children with MR of unknown etiology than for the children with MR of known etiology. As a consequence, many of them maintain their lives at a social adaptive level that is far under their real potential. Therefore, physicians must be familiar with their clinical characteristics in its developmental process for early diagnosis and intervention. However, according to our literature reviews, there were few reports about the clinical characteristics of children with MR of unknown etiology.

The purpose of this study was to investigate the clinical characteristics of children with MR who had no clear etiology for early recognition and intervention.

MATERIALS AND METHODS

Subjects

One hundred sixty-four children (108 male, 56 female) with MR participated in this study. Subjects were retrospectively selected from 470 children who visited the Department of Physical Medicine & Rehabilitation, Ajou University Medical Center with a developmental delay in the areas of gross motor, fine motor and language from June 1994 to February 1997. Children were admitted to this study when they were assessed with MR by evaluating intellectual function at the age of 36 months or older. Diagnosis of MR was made according to the 1992 American Association on Mental Retardation's definition for MR (5, 6). Mean (±SD) age

Table 1. Primary diagnosis of children with mental retardation

Primary diagnosis	Number of patients (%)
Mental retardation of unknown etiology*	80 (48.8)
Cerebral palsy	38 (23.2)
Down syndrome	20 (12.2)
Autistic disorder	9 (5.5)
Attention-Deficit/Hyperactivity disorder	5 (3.0)
Epilepsy	4 (2.4)
Chromosomal anomaly	4 (2.4)
Others†	4 (2.4)
Total	164 (100)

*: Mental retardation without clear etiologies and associated behavioral problems. †: Linear and whorled nevoid hypermelamosis (1), reactive attachment disorder (1), congenital heart disease (2).

of subjects at the time of selection for this study was 64.56 ±10.44 months (range from 36 months to 84 months).

Primary diagnoses of subjects with MR were MR of unknown etiology (80 children, 48.8%), cerebral palsy (38 children, 23.2%), Down syndrome (20 children, 12.2%), autistic disorder (9 children, 5.5%) and so on (Table 1). The diagnostic work-up of MR in this study was individualized. We performed a chromosomal analysis including the Fragile X study, and screening for amino acids and organic acids when indicated. Similarly, we performed a computed tomographic (CT) scan or magnetic resonance imaging (MRI) of the brain when they were clinically indicated. All 38 children with MR associated with cerebral palsy showed abnormal findings in brain MRI and/or brain CT. All 20 children with MR associated with Down syndrome were confirmed by the chromosomal study. The diagnoses of autistic disorder in nine children were made by a child psychiatrist on a consultation basis.

In this study, we defined children with MR of unknown etiology as those without clear etiologies for MR despite extensive evaluation and were not associated with pathological behavioral problems such as pervasive developmental disorders and attention-deficit/hyperactivity disorder. Inclusion criteria of MR of unknown etiology were as follows. 1) Child with MR according to above-mentioned criteria. 2) Child with acceptable gross motor development including gait for their age at the time of selection for this study without showing any abnormal movements or postural patterns. 3) Child without any of following conditions : family history of mental retardation, prematurity (gestational period ≤ 37 weeks), low birth weight (birth weight ≤ 2,500 g), perinatal asphyxia (APGAR score < 5 at 1 min or 5 min or respiratory difficulty requiring an immediate neonatal resuscitation and/or ventilator care), abnormal anthropometric measurements of growth (height, weight, and head circumference), seizure disorders, head injury, infections of brain, malnutrition, syndrome disorders including Fragile X syndrome and other chromosomal disease, inborn error of metabolism, environmental deprivation, and any history of known risks for MR. Radiological findings of the brain were not included in these criteria. Eighty children with MR of unknown etiology met all three inclusion criteria.

Procedure

Subjects'clinical characteristics were reviewed and analyzed according to their primary diagnosis. Clinical characteristics selected for analysis were age, sex, a chief complaint on the first visit to authors, age at the beginning of independent walking, intelligence quotient score, percent age of fine motor and activities of daily living (ADL), and language function.

The assessment of intellectual functioning was conducted with instruments such as a mental score of Bayley Scales of Infant Development-II (7), Korean Pictorial Test of Intelligence (8), and a Korean Wechsler scale depending on the child's age.

To determine fine motor and ADL function, we used the Developmental Age Referenced Breakdown Assessment Schedules (DARBAS) (9). We assessed language function by the Peabody Picture Vocabulary Test-Revised (10) or Oral Receptive-Expressive Emergent Language Scale (11) for children who needed to be evaluated for delayed speech development.

Statistical analysis

Data are summarized as mean ±SD. We performed an one-way analysis of variance (ANOVA) for the statistical analysis of clinical characteristics according to the primary diagnosis of MR. If the results were statistically significant, we then used multiple-comparison test using the Least-significant difference method to determine which of the differences in means were the true differences. The statistical package was SPSS Win (SPSS, 1994).

RESULTS

Children with MR of unknown etiology were more common in males. Male-to-female was 3 : 1 (Table 2).

Delayed language development was the most common complaint in children with MR of unknown etiology. Among 80 children with MR of unknown etiology, 49 children (61.3%) were referred to our clinic for the evaluation of delayed language development (Table 3). On the other hand, the chief complaint of a questionable subaverage intellectual functioning was found only in 10 children (12.5%).

Most children with MR of unknown etiology were delayed walkers. On average, the children with MR of unknown eti-

Table 2. Male-to-female ratio in children with mental retardation by major primary diagnosis

Primary diagnosis	No. of boys	No. of girls	Male-to-female ratio
MR of unknown etiology*	60	20	3 : 1
Cerebral palsy	18	20	0.90 : 1
Down syndrome	9	11	0.82 : 1
Autistic disorder	8	1	8 : 1

*: Mental retardation without clear etiologies and associated behavioral problems.

Table 3. Chief complaints of children with mental retardation* of unknown etiology on first visit

Chief complaint	Number of patients (%)
Delayed language development	49 (61.3)
Delayed motor development	14 (17.5)
Questionable subaverage intellectual functioning	10 (12.5)
Others	7 (8.8)
Total	80 (100)

*: Mental retardation without clear etiologies for mental retardation and associated behavioral problems.

Table 4. Age of children with mental retardation at the beginning of independent walking by major primary diagnosis (n=86)

Primary diagnosis	Group	No. of patients	Age at the beginning of Independent walking (mo)	$p^{\dagger}$
Autistic disorder	A	7	13.1 ± 2.4	0.0010
MR of unknown etiology*		62	19.8 ± 11.7	
Down syndrome	B	5	24.6 ± 7.2	
Cerebral palsy		12	34.0 ± 17.2	

*: Mental retardation without clear etiologies for MR and associated behavioral problems. †: There is significant difference (p=0.0010) in age of children with mental retardation at the beginning of independent walking between two groups (A, B).

Table 5. Intelligence quotient (IQ) score in children with mental retardation in two major primary diagnosis (n=93)

Primary diagnosis	Number of patients	Intelligence quotient
MR of unknown etiology*	80	55.4 ± 18.4
Cerebral palsy	13	51.0 ± 15.0

*: Mental retardation without clear etiologies for MR and associated behavioral problems. There is no significant difference in IQ between mental retardation and cerebral palsy (p>0.05).

ology began to walk at 19.8±11.7 months of age (Table 4).

Most children with MR of unknown etiology were mild cases. The mean intelligence quotient score in those children was 55.4±18.4 (Table 5).

Table 6. Percent fine motor and activities of daily living (ADL) function age of children with mental retardation by major primary diagnosis (n=138)

Primary diagnosis	Group	No. of patients	Percent fine motor age (%)†	Percent ADL function age (%)‡	$p^{\S}$
Cerebral palsy	A	38	38.2±27.7	50.3±25.3	< 0.05
Down syndrome	B	20	55.7±21.9	70.9±31.7	
MR of unknown etiology*		80	61.8±22.1	67.1±22.3	

*: Mental retardation without clear etiologies and associated behavioral problems. †: Percent fine motor age={fine motor age (mo)/ chronological age (mo)} ×100, ‡: Percent ADL function age={ADL function age (mo)/ chronological age (mo)} ×100, §: There is a significant difference of percent fine motor age (p=0.0017) and percent ADL function age (p=0.0141) of children with mental retardation between two groups (A: cerebral palsy, B: Down syndrome, MR of unknown etiology).

Table 7. Percent receptive and expressive language age of children with mental retardation by major primary diagnosis (n=68)

Primary diagnosis	No. of patients	Percent receptive language age (%)†	Percent expressive language age (%)‡
Cerebral palsy	13	41.2±19.7	38.6±20.4
Down syndrome	5	54.9±18.0	46.1±16.5
MR of unknown etiology*	50	54.1±17.4	48.1±17.4

*: Mental retardation without clear etiologies and associated behavioral problems. †: Percent receptive language age={receptive language age(mo)/ chronological age (mo)} ×100. There is a significant difference (p= 0.0685) of percent receptive language age between two groups (A cerebral palsy, B: Down syndrome, mental retardation). ‡: Percent expressive language age={expressive language age (mo)/ chronological age (mo)} ×100. There is no significant difference (p=0.2457) of percent expressive language age among three major primary diagnosis.

Children with MR of unknown etiology showed a development delay in the areas of fine motor (61.8±22.1%), ADL (67.1±22.3%), and language function (54.1±17.4% in receptive language, 48.1±17.4% in expressive language) when compared with normal subjects of the same chronological age (Table 6, 7).

DISCUSSION

This study revealed that the clinical characteristics of children with MR of unknown etiology were as follows: 1) MR of unknown etiology was 48.8% of all MR. 2) MR of

unknown etiology was more common in males. 3) Delayed language development was a leading factor that made the parents of children with MR of unknown etiology seek help from physicians. However, most of the children with MR of unknown etiology showed a relatively uniform delay in several areas of development. 4) Most children with MR of unknown etiology were delayed walkers. 5) Most children with MR of unknown etiology were mild cases.

MR of unknown etiology comprised 48.8% of all kinds of MR, which was in accord with previous reports (1, 5, 6). MR with unknown etiology does not mean that a cause does not exist. Continuing effort is required to identify the etiology of MR. Currently unknown etiology of MR will be eventually revealed with the advancement of medical technology. It is quite possible that some of these cases could be related to developmental disturbances in neuronal connectivity mediated by dendritic, axonal, synaptic, or glial mechanisms, a concept that has been termed *hypoconnection* to indicate the potential neurobiological origin of inefficient information processing. The precise etiology of these disturbances in connectivity remains to be elucidated through better understanding of the genetic and environmental processes that contribute to the development of the brain (12).

MR of unknown etiology was more common in males and the male-to-female ratio was 3:1. The literature review revealed that the male-to-female ratios for mild MR ranges from 40% excess of males in the Netherlands to 80 % excess in Sweden (13, 14). This might reflect a difference in registration and case ascertainment or a greater susceptibility of the male central nervous system. Further studies are required for the discovery of exact causes of male predominance in MR of unknown etiology (15-17).

According to this study, most of the children with MR of unknown etiology showed a relatively uniform delay in several areas of development. However, delayed language development was most problematic to their parents and was a leading cause for more than 50% of children with MR of unknown etiology presented to physicians by their parents for evaluation. Children with MR of unknown etiology showed 50-70% of developmental levels in the areas of fine motor, ADL, and language function when compared with normal subjects of the same chronological age. However, 61.3% of children with MR of unknown etiology was referred to the clinic for evaluation of delayed language development. These findings suggest that delayed language development is more noticeable than delayed development of fine motor and ADL function. Since most children with MR of unknown etiology attain independent walking by the age of two years, their parents seem to regard their children as delayed walkers and as a matter of little importance. In this study, the mean age at the beginning of independent walking for children with MR of unknown etiology was 19.8 ± 11.7 months. Shapiro (1979) studied 152 profound cases of mentally retarded children (IQ below 25) without an acquired or a progressive degenerative disease, and found that their walking began at the mean age of 30 months (18). It is known that cognition is a less important determinant in walking than is basic neurological integrity. It is evident that motor assessment alone cannot determine MR (19). Therefore, a screening for the presence of MR is considered necessary as a part of evaluation for children with delayed language development.

Most children with MR of unknown etiology show a mild MR. A recent review of 13 epidemiological studies identified approximately 30 percent of cases as severe MR and approximately 50 percent of cases as mild MR (17). In this study, mean IQ score of children with MR of unknown etiology was 55.4 ± 18.4. These findings indicate that a great majority of people with mental retardation can be productive and become full participants in society. Early appropriate intervention and educational services in infancy and throughout the developmental period and beyond will enable the children with MR to develop to their fullest potential (5, 6). Accordingly, physicians must be familiar with the clinical characteristics of children with MR of unknown etiology for early diagnosis of MR. The knowledge on clinical characteristics of MR of unknown etiology will help clinicians to detect this condition early. Early diagnosis of mental retardation must be followed by the identification of supports needed for the adaptive skills, medical, physical or psychological services, and modification of individual's environment by a comprehensive pediatric rehabilitation.

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