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SURVEY OF DUCHENNE TYPE AND CONGENITAL TYPE OF MUSCULAR DYSTROPHY IN SHIMANE, JAPAN[1]

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Summary Duchenne muscular dystrophy and congenital muscular dystrophy (Fukuyama type) were analyzed clinically, genetically and epidemiologically in Shimane Prefecture in the Western Honshu Island of Japan. Cases were collected from all available sources and the diagnosis was reexamined by our group, yielding a total of 83 patients with various myopathies.

Thirty-two patients with Duchenne muscular dystrophy were found. Their clinical manifestations were not different from cases occurring elsewhere in Japan. The incidence rate of this type was 20.8×10^{-5}. Parental consanguinity of the cases was noted in 18.5%, considerably higher than control families.

As to the Fukuyama type of congenital muscular dystrophy, 11 patients were identified. The incidence rate was 5.60×10^{-5}. There was no doubt that an autosomal recessive pattern of inheritance was involved in these patients. The gene frequency was estimated as 0.0075.

INTRODUCTION

Duchenne muscular dystrophy and congenital muscular dystrophy are the most common and clinically severe myopathies in childhood. According to Araki (1967), the prevalence rate of progressive muscular dystrophy pooling all types is $2.6–5.5 \times 10^{-5}$ in Japan, of which 44.5% is classified as Duchenne type. Although far less frequent than Duchenne type, a congenital type of muscular dystrophy first reported by Fukuyama *et al.* (1960) is widely known among Japanese pediatricians. This type is supposed to be recessively heritable, but there is no report about its frequencies in the population.

The present report describes clinical, genetic and epidemiologic patterns of the stated two types of muscular dystrophy in Shimane Prefecture, located in Western Honshu Island of Japan.

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MATERIALS AND METHODS

In order to find patients possibly suffering from myopathies, questionnaires were sent to all the nurse-teachers in 118 infant schools, 318 primary schools and 141 junior high schools in Shimane Prefecture, asking whether there were individuals who had motor troubles like myopathies. In addition, records in two public institutions for children, three hospitals for handicapped children and two protecture institutions in Shimane Prefecture were also surveyed for similar cases. The population survey was done from January, 1975 through June, 1975. The provisional cases with suspected myopathy were collected from people of all ages.

All patients were examined neurologically and electromyographically and serum levels of creatine-phosphokinase (CPK) were determined. Muscle biopsies were made for definite diagnosis in some cases. The medical examination was finished in November, 1975.

RESULTS

The questionnaires were all returned and yielded 104 provisional cases, whereas 58 cases were found in the record surveys. Reevaluation of the diagnosis revealed that a total of 83 patients were suffering from various types of muscular dystrophy as seen in Table 1. The population in Shimane Prefecture was 768,876 in 1975. The prevalence rate of muscular dystrophy, all types pooled, was approximately 10.7×10^{-5} for November, 1975.

Duchenne muscular dystrophy

Thirty-two Duchenne patients were found. All cases were males, their age ranged mostly 5–19.

Clinically, (1) the mean age of onset was 4.7 ± 1.37 years, (2) all patients except one manifested the disease with gait disturbances as initial symptoms, (3) 23 bed-patients became unable to walk between 9–15 years of age, (4) pseudohypertrophy was seen in all patients, (5) subnormal intelligence was noted in 21 patients.

Table 1. Numbers of patients with muscular dystrophy by type and sex and numbers of families of patients exhaustively collected in Shimane Prefecture, November, 1975.

	Duchenne type	Congenital type		Limb-girdle type	Facio-scapulo-humeral type	Others	Myotonic dystrophy	Total
		Fukuyama type	Others					
Male	32	5	4	10	1	1	2	54
Female	0	6	1	12	2	2	5	29
Total	32	11	5	22	3	3	7	83
No. of families	27	7	5	15	3	3	3	63

Table 2. Incidence of Duchenne muscular dystrophy among male live-births between 1956–1970.

Year of birth	No. of male live-births	No. of patients	Incidence rate (10^{-5})
1956–1960	26,992	7	259
1961–1965	29,593	4	135
1966–1970	34,572	8	231
Total	91,157	19	208

Table 3. Consanguineous marriages among parents of Duchenne muscular dystrophy and Fukuyama type congenital muscular dystrophy.

	Duchenne type	Congenital type	Control in Shimane
No. of families	27	7	480
First-cousins	3	1	12 (2.5%)
Half-cousins	2	1	15 (3.1%)
Second-cousins	0	0	3 (0.6%)
Total	5 (18.5%)	2 (28.6%)	30 (6.2%)

When plotted against a map of the prefecture, the addresses of the patients revealed no focus of high incidence. Incidence rate of this type among the 91,157 male aged between 5 and 19 (born in 1956–1970 inclusive) was 20.8×10^{-5} or about 1 in 4,800 male youths (Table 2). The rates did not change by year periods of the birth.

All the patients were comprised in 27 families. Consanguinity up to second cousin mating was observed in 5 pairs of the parents (Table 3). Consanguinity rate was 18.5% and the coefficient of inbreeding was 0.0092. According to the family patterns of the patients, 4 mothers were definite carriers, whereas 3 were probable and the remaining 20 were possible carriers.

Fukuyama-type congenital muscular dystrophy

A total of 16 patients were classified as having congenital myopathies. Eleven of the 16 patients, 5 males and 6 females, belonged to the group of Fukuyama-type congenital muscular dystrophy.

Clinically, (1) all the patients were unable to walk alone, (2) muscular weakness were severe and proximally dominant, (3) facial muscular involvement, joint contractures and severe mental retardation were noted in all the patients.

The geographical distribution of 11 patients revealed no particular pattern.

Ten of 11 patients were aged from 5 to 19. Incidence of this group among a total of 178,457 population aged between 5 and 19 (born in 1956–1970) was 5.60×10^{-5} or about 1 in 18,000 youths (Table 4).

All the patients were comprised in 7 families. Consanguinity up to second cousin mating or more was observed in 2 pairs of parents (Table 3). Consanguinity rate was 29.6% obviously elevated than the proportion in control parents from the same

Table 4. Incidence of Fukuyama type congenital muscular dystrophy among live-births between 1956-1970.

Year of birth	No. of live-births	No. of patients (male:female)	Incidence rate (10^{-5})
1956-1960	52,296	5 (3 : 2)	956
1961-1965	58,285	4 (0 : 4)	686
1966-1970	67,876	1 (1 : 0)	179
Total	178,457	10 (4 : 6)	560

population. Of a total of 18 sibs in 7 families 11 were patients. Segregation ratio, which was calculated according to Weinberg's formula, was found to be 0.0364, although its validity was questionable due to a small sample size.

DISCUSSION

Patterns of Duchenne type as well as Fukuyama type of muscular dystrophy, particularly their frequencies, were evaluated in Shimane Prefecture in Japan.

As to the frequency of Duchenne type diversified figures have been published. A low incidence, namely 1 in 100,000 live births *i.e.*, 1 in 50,000 live-born male infants, was mentioned by Pearson (1973). Morton and Chung (1959) estimated the incidence for Wisconsin to be 1 in 3,000 live births. A similar figure can be computed from the studies of Stephens and Tyler of Utah (1951).

Zellweger and Antonik (1975) also found 1 case in 3,300 male live births. In Japan, Miyazaki (1963) estimated the prevalence rate for Fukuoka City to be 4×10^{-5}, which was similar to those from the studies of Walton (1955). From records in the many public hospitals, Araki (1967) estimated the prevalence rate of progressive muscular dystrophy in Japan to be $2.6\text{–}5.5 \times 10^{-5}$, of which 44.5% had Duchenne muscular dystrophy. According to our work in Shimane Prefecture, the incidence of Duchenne muscular dystrophy was 20.8×10^{-5} or about 1 in 4,800 male youths. Assuming that all patients under the age of 19 had survived the disease, the estimates might be similar to the incidence among male live births.

Duchenne muscular dystrophy is generally considered to be inherited as an X-linked recessive trait. However, there have been a few reports of cases purportedly transmitted by an autosomal recessive gene. Miyoshi *et al.* (1975) estimated from their pooled data that X-linked recessive, new mutation and autosomal recessive types occurred with the proportion roughly 68 : 25 : 14. The consanguinity rate of 18.5% encountered in the parents of our Duchenne patients was remarkably higher than 6.3% in the control families. This may probably indicate that simple recessive cases were included in our material which were indistinguishable from X-linked Duchenne patients.

Congenital muscular dystrophy reported by Fukuyama *et al.* (1960) is the most common type of congenital dystrophies observed in Japan. This is characterised

by (1) transmission by an autosomal recessive gene, (2) slow progression, (3) proximal muscular weakness with facial muscular involvement, (4) early onset of joint cotractures, and (5) frequent mental retardation. All the patients so diagnosed in Shimane Prefecture exhibited typical picture of this group.

Its incidence rate was estimated as 5.60×10^{-5} or about 1 in 18,000 youths, but as some patients might posssibly died without surviving until the age of 5, this figure is considered to be low. No data pertaining to the frequency of this disease was reported thus far.

The consanguinity rate of 28.6% in Fukuyama type was remarkably higher. The both sexes were nearly equally affected, and although acceptable segregation ratio was not available, there was little doubt that an autosomal recessive pattern of inheritance was involved in these patients. Based on records in many public hospitals, Kondo *et al.* (1974) made a genetic analysis of the disease and accepted the stated pattern of inheritance. They estimated the gene frequency of this type to be 0.94–1.56%.

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