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Congenital, hypotonic-sclerotic muscular dystrophy

TETSUO FURUKAWA AND YASUO TOYOKURA

From the Department of Neurology, University of Tokyo, Tokyo, Japan

SUMMARY Four cases of congenital, hypotonic-sclerotic muscular dystrophy are presented. The patients showed clinically prominent features described by Ullrich, i.e. congenital muscle weakness, hypotonia, and hyperextensibility of distal joints, contractures of proximal joints, high-arched palate, hyperhidrosis, posterior protrusion of calcaneus, and no progression. Muscle biopsies revealed dystrophic changes. Ullrich suggested that this condition was a new entity, but the disease has received little attention. In the present cases superior intelligence and tendency to recurrent upper respiratory tract infections were stressed as characteristics of this disorder. Insufficient cellular immunity was suspected and this may contribute to the recurrent upper respiratory tract infections and pneumonia often observed. This disease is considered a distinct entity of multisystemic involvement inherited as an autosomal recessive trait.

In 1930 Otto Ullrich described 2 patients who had clinically prominent features, i.e. congenital muscle weakness, hypotonia, and hyperextensibility of distal joints, contractures of proximal joints, high-arched palate, hyperhidrosis, posterior protrusion of calcaneus, and no progression. He suggested that his cases constituted a new entity not previously described and coined 'kongenitale, atonisch-sklerotische Muskeldystrophie' for this condition.

Since his descriptions (Ullrich, 1930a, b) some case reports have appeared in the German literature (Stoeber, 1939; Gött and Josten, 1954; Schneider, 1957; Rotthauwe and Kowalewski, 1969); however, scant attention has been paid to this disorder in other countries. No reports concerning this disorder can be found in the English literature.

Recently we encountered 4 cases of it and examined them from clinical and immunological standpoints.

The purpose of this report is to present additional clinical and immunological characteristics of this disease and to establish the condition as a distinct entity of multisystemic involvement inherited as an autosomal recessive trait.

Case reports

CASE 1

A 16-year-old boy, whose parents were cousins, and whose mother had congenital total hemiatrophy of left side, and complained of slight difficulty in walking. Pregnancy was uneventful, but fetal movements were weak. He was born at term by normal delivery. Body weight was 2600 g. Immobility of both hip joints and torticollis were noted at 2 to 3 months of age. He was floppy and could not crawl. His mother had difficulty having him put on his gloves, because his fingers were atonic and easily hyperextended. At age 5 he could stand if supported, but it became impossible in a few months. Marked kyphoscoliosis appeared and progressed slowly, but muscle weakness was not progressive. He developed recurrent upper respiratory tract infections in childhood, and was admitted to another hospital because of severe pneumonia at the age of 2 months. He attended a school for the physically handicapped and impressed the teachers with his apparently high intelligence.

Physical examination, at age 16, revealed prominent kyphoscoliosis and torticollis, as shown in Fig. 1. Hip, shoulder, and knee joints were contractured bilaterally and could not be extended, and hand, finger, and foot joints could be easily hyperextended. Fingers and toes were long and slender. The calcaneus was protruded posteriorly. The cranial nerves were intact. The palate was high and arched. All the tendon reflexes were decreased and no pathological reflexes were elicited. Sensation was intact. Perspiration was profuse, especially in the palms and soles. Muscular atrophy and weakness were diffuse but rather distally dominant. IQ was

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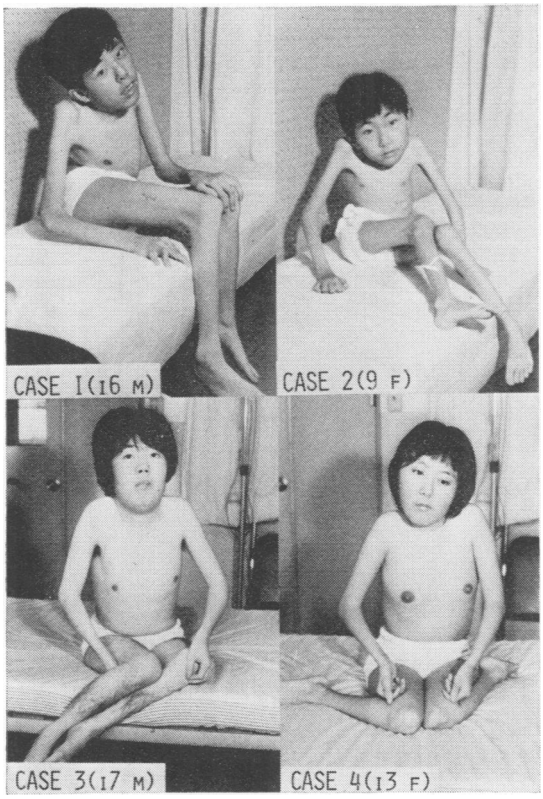

Fig. 1 *Photographs of patients.*

108. Electromyographic (EMG) examination revealed action potentials of low amplitude and short duration, which were interpreted as myogenic pattern. Serum creatine kinase (CK) was normal. Routine haematoanalysis, urinalysis, and serum biochemistry were within normal limits. Muscle biopsy from the right rectus femoris showed an advanced stage of dystrophic changes. The majority of the muscle fibres had degenerated and were replaced by fat.

CASE 2

The 9-year-old sister of case 1 was born at term as a floppy baby (3290 g). This patient had torticollis and contractures of bilateral coxal joints at birth. Luxatio coxae congenita was the diagnosis at that time. She had never crawled or stood. The torticollis, kyphoscoliosis, and contractures of proximal joints became prominent as she grew up, but muscle weakness was not progressive. She had recurrent upper respiratory tract infections. The clinical features were similar to those of her brother. She was shy but intelligent. EMG showed a myogenic pattern and muscle biopsy findings of the left rectus femoris were much the same as those of her brother. Routine laboratory studies were within normal limits.

CASE 3

A 17-year-old boy was born after full term pregnancy. The family history was not contributory and there was no consanguinity. He could sit upright for several minutes at 1 year of age. He was diagnosed as luxatio coxae congenita in another hospital. At the age of 2 he began to walk unsteadily, but became unable to stand at 5. His lordoscoliosis became prominent. His hip and shoulder joints were contractured, but hands and feet were atonic and hyperextensible. High-arched palate, calcaneus protrusion, and hyperhidrosis were observed. EMG was myogenic and muscle biopsy of the right rectus femoris showed dystrophic changes. Most of the muscle fibres were replaced by adipose tissue. Serum CK was normal. Sural nerve biopsy was normal. He did well at school. IQ was 117. He was said to have had the common cold many times in childhood.

CASE 4

A 13-year-old girl, whose parents were cousins was born at term as a floppy baby (2300 g) and began to crawl at the age of 4 years. The patient had torticollis and kyphoscoliosis since her birth. An operation was performed to correct the torticollis. She was unable to stand or walk, but at 5 she was able to walk on her knees. Her disease was not progressive and she could move by crawling. She was an intelligent and cooperative girl, IQ 110. She had torticollis and kyphoscoliosis, high-arched palate, distal hypotonia, hyperhidrosis, calcaneus protrusion, and hyporeflexia. Serum CK was normal. EMG revealed myogenic pattern. A biopsy was obtained from the right rectus femoris muscle, and showed histological changes which were much milder than those of the former patients. Rounded muscle fibres of uneven size were observed. Nuclei were centrally placed. In longitudinal sections dystrophic fibres were seen together with normal fibres with striations. Fig. 2 shows longitudinal section of degenerating muscle fibres. Normal muscle fibres were also seen along the dystrophic fibres.

Special investigations

Tuberculin test was performed by routine method. In case 1 the tuberculin test was said to be positive after BCG injection in childhood. But all the cases showed negative reaction.

DNCB (2,4-dinitrochlorobenzene) skin test was also performed. 0·01 ml 1% acetone solution of DNCB was applied to the inner surface of the right

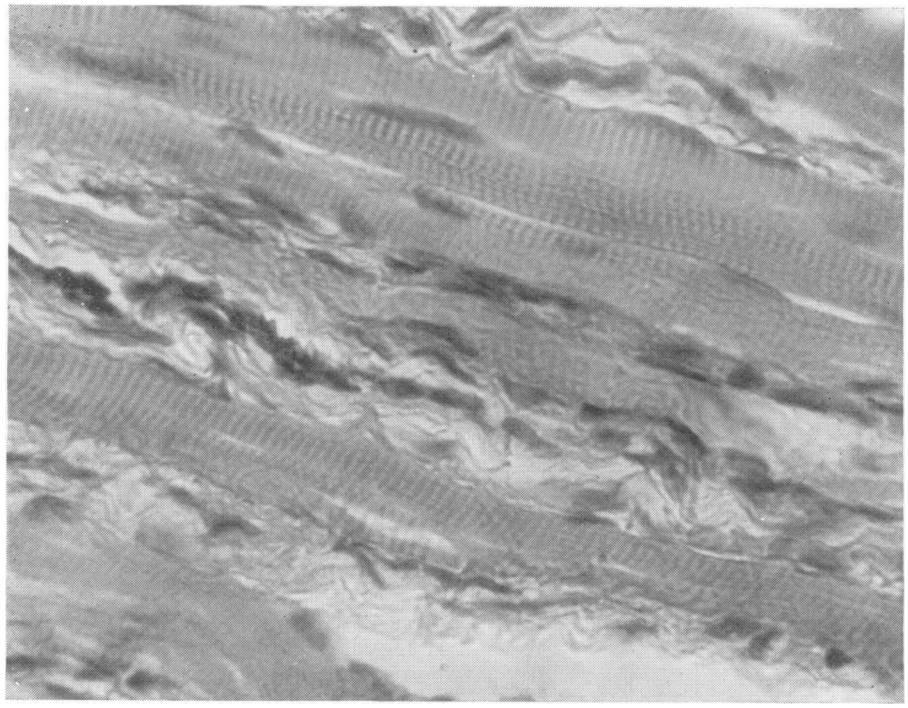

Fig. 2 *Longitudinal section of rectus femoris muscle of case 4. Degenerating muscle fibres are shown. Normal muscle fibres with striations are seen along the dystrophic fibres. (Haematoxylin and eosin × 400.)*

Table *Tuberculin test, DNCB test, and serum immunoglobulins of patients*

	Case 1	*Case 2*	*Case 3*	*Case 4*
Tuberculin test	BCG(+)?→(0×0/0×0)	(0×0/0×0)	(0×0/0×0)	(0×0/0×0)
DNCB test	1+	negative	negative	negative
Serum immunoglobulins (mg/100ml)				
IgG(960-2540)	2205	2415	1920	1720
IgA(168-306)	159	154	91	169
IgM(99-215)	131	154	115	191

(Normal ranges are shown in parentheses)

upper arm for 24 hours. After 2 weeks 0·01 ml 0·1% solution was applied to the left side and the skin reaction was checked after 48 hours. In case 1 only was slight erythema observed (1+) but the others showed no skin changes (−) (Table).

Serum immunoglobulins were determined (Table). IgA was on the borderline or decreased in these cases. IgG and IgM were within normal limits.

Urinary excretion of hydroxyproline was 87·8 mg per day in case 1 and 64·5 mg in case 2. These values were almost normal. Amino acid analysis of urine in cases 3 and 4 was normal.

Discussion

Since the original descriptions of Ullrich in 1930, similar cases have been recorded in the German literature. In 1939 Stoeber considered Ullrich's cases a clinical entity and classified congenital, hypotonic-sclerotic muscular dystrophy as a specific type within the category of congenital muscular dystrophy.

The characteristic features of this disorder are as follows: (1) disorder since birth, (2) acroatonia, (3) truncal contractures, (4) relatively spared muscles innervated by cranial nerves, (5) taille de guêpe, (6) posterior protrusion of calcaneus, (7) high-arched palate, (8) normal or active tendon reflexes, (9) strongly positive facialis phenomenon, (10) hyperhidrosis, (11) well-developed intelligence, and (12) no progression, but rather a recovery of motor function. The present cases are compatible with these criteria except (8) and (9).

Except Ullrich's cases Chvostek phenomenon was

negative. Tendon reflexes were normal or decreased in most reported cases. Therefore, (8) and (9) must be deleted from the criteria of clinical signs and symptoms of this disorder.

One of the characteristic symptoms of this disorder, which was not stated by Ullrich but later added by Gött and Josten (1954), colleagues of Professor Ullrich, is a tendency to recurrent infections of the upper respiratory tract. Case 1 of Ullrich's report showed recurrent upper respiratory tract infections and died of pneumonia. His second case developed recurrent bronchopneumonia and died of pneumonia, too. One of Gött and Josten's cases developed pneumonia three times and the other had recurrent infections of the upper respiratory tract and pneumonia. They considered this tendency to be a disposition of this disorder. Schneider (1957) also stressed this tendency as one of the characteristics of this disease. In all cases the cause of death in the cases described in the literature was always pneumonia.

Cases 1, 2, and 3 also had such a tendency. Tuberculin test was negative in all 4 cases. Among the previously described cases, Ullrich's case 1 showed negative tuberculin test. DNCB test was 1+ in case 1, but negative in the other 3 cases. These data suggest decreased cellular immunity in these patients and can explicitly explain the tendency to recurrent infections. Among serum immunoglobulins IgA was slightly decreased.

Intelligence in patients with this disorder merits special attention. All the present cases did well at school. Ullrich reported that these patients had well-developed intelligence. His intention was supposed to suggest that mental retardation was not the case in this disorder as is often observed in congenital hereditary disorders. However, all the observed cases suggested high intelligence. For example, the case of Y. Toyokura, T. Takasu, N. Yanagisawa, and H. Tsukagoshi (unpublished observation) attained straight 4's (5 to 1 grades) in ordinary primary school despite his great physical handicaps. K. Nihei's patient (personal communication 1975) showed 150 in IQ test. Y. Nakano's case (1976, personal communication) did well at school. IQ's in our patients are considered to be much lower than their real IQ's because of their physical handicaps and undesirable environments. Superior intelligence might be characteristic of this disease as seen in some hereditary diseases, such as retinoblastoma (Thurrell and Josephson, 1966; Williams, 1968) and autosomal recessive form of torsion dystonia (Eldridge *et al.*, 1970).

As stated above, Ullrich's muscular dystrophy has been recorded only in the German literature and no reports concerning this disorder can be found in the English literature. Though Ullrich's muscular dystrophy has clinically prominent features, these signs and symptoms are also observed in various other diseases, such as benign congenital myopathy, congential muscular dystrophy, or arthrogryposis multiplex congenita. This might be because no reports have been published and this disease has not been regarded as a distinct entity. However, this disorder showed not only various characteristic clinical features, but also a tendency to upper respiratory tract infections with insufficient cellular immunity. This is specific of this disorder and is not frequently observed in ordinary muscular dystrophy. Therefore, Ullrich's muscular dystrophy is considered a distinct entity of multisystemic involvement.

Although histological changes were similar to those seen in ordinary muscular dystrophy and the term 'congenital, atonic-sclerotic muscular dystrophy' was coined by Ullrich, serum enzymes did not increase and muscle weakness was not progressive. These are unusual in muscular dystrophy. This disease is considered a distinct entity, and clarification of underlying biochemical abnormalities awaits further investigations.

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Requests for reprints to Dr Tetsuo Furukawa, Department of Neurology, Institute of Brain Research, School of Medicine, University of Tokyo, Hongo, Tokyo, Japan.