Case Report

A CASE OF ATYPICAL DUCHENNE TYPE MUSCULAR DYSTROPHY WITH FRAGILE X

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Summary The patient was a 9-year-old boy. He began to walk at the age 1 year and 8 months and began to speak at the age of 2 years, suggesting retarded mental and motor development. A diagnosis of DMD was made when he was 7 years old. On admission, the patient exhibited a peculiar thin and long face, large auricles, narrow palate, malalignment of the teeth, epicanthus, saddle nose, and simian lines in addition to symptoms consistent with DMD. Chromosome analysis showed fragile X at Xq27 at a frequency of 20%. His mother also showed fragile X at the same position. Since the atypical features of this DMD patient are all explained as fragile X syndrome, this case was considered to be a very rare instance of DMD whose clinical pictures were modified by fragile X syndrome.

Key Words Duchenne muscular dystrophy, chromosome aberrations, fragile X, DMD, FRAXA

INTRODUCTION

Reports of chromosome aberrations in patients with Duchenne type progressive muscular dystrophy (DMD) have been very scarce, with only a few cases of reciprocal translocation of p21 of X chromosome with autosomes No. 1, 2, 3, 4, 5, 6, 9, 11, and 21 having been documented. Concomitant presence of DMD and fragile X has not been known. In this report, a case of atypical DMD complicated by fragile X is described.

CASE REPORT

The patient was a 9-year-old boy with the primary complaint of dysbasia. The family history included on consanguine marriage or analogous illnesses. His

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younger brother was a 6-year-old boy, who also had slight mental retardation, but showed no symptoms of muscular dystrophy. His mother had no history of abortion and he was born by cesarean section at 40 weeks of gestation due to pelvic presentation. The birth weight was 2,830 g and no asphyxia was noted. His mother was 25 years old and his father was 29 years old at his birth.

The patient contracted otitis media 1 month after birth. No history of convulsion was reported. Weak sucking was noticed in the infantile period. Head control was at 3.5 months, sitting at 8 months, crawling at 12 months, and walking without support at 1 year and 8 months of age. He began to speak at the age of 2 years. About this time, he was first noted to fall readily and to have abnormal gait, and was examined at a university hospital, where retardation of the mental and motor development was indicated. Dysbasia deteriorated gradually thereafter, and a diagnosis of progressive muscular dystrophy was made at 7 years of age. Standing became difficult around this time.

At 8 years of age, he first visited the Department of Neurology, Nishitaga Byoin National Hospital. Neurological examinations revealed retarded mental and verbal development and a DQ (Suzuki-Binet test) of 40. The patient had a cheerful personality and showed no signs of autism. The gait was staggering,

Fig. 1. Patient profile showing characteristic facial expression and mild muscle atrophy in the upper arms and scapular regions.

and Gowers' sign was positive. Muscle weakness, which was dominant in the facial and proximal muscles. Reduced muscle tone and mild muscle atrophy of the scapular regions, face and upper arms were also noted. The grip strength was 60 mmHg in the right and 30 mmHg in the left. Pseudohypertrophy of the gastrocnemius muscle, contracture of the knees and foot joints, and disappearance of deep tendon reflex except for achilles tendon reflex were observed, but there was no pathologic reflex, impairment of urination nor myotonia. The functional impairment was stage 6 according to the scale of the Ministry of Health and Welfare.

Minor congenital anomalies included narrow palate, malalignment of the teeth, single palmar crease, epicanthus, and saddle nose. Giant testis was absent. The face was thin and long and showed large auricles and a myopathy-like facial expression.

Clinical laboratory studies on admission were unremarkable except for marked increase in GOT (62.1 IU/L), GPT (142 IU/L), LDH (1,080 IU/L), CPK (3,382 IU/L), ALD (19.8 U/L), and urinary creatinine (524 mg/day). Electrocardiography showed high R and deep Q in V_1 characteristic of progressive muscular dystrophy. The results of craniometry and CTR were within the normal ranges, and CT showed no abnormalities. Needle electromyography showed myogenic changes. The vital capacity was markedly reduced, but this measurement was considered to be inaccurate because of the mental retardation and weakness of facial muscles. High amplitude slow rhythms, 5–6 Hz and 100–120 μ V, were observed in electroencephalography. Muscle biopsy revealed dystrophic changes; irregularity in the size of muscle fibers and marked fibrosis. No cell infiltration was noted.

For chromosome analysis, peripheral blood (0.2 ml) was incubated for 96 hr in folic acid-free MEM-FA medium (2 ml) containing 5% fetal calf serum and

Fig. 2. Chromosome gap at Xq27. An arrow indicates fragile X.

2% PHA or the same medium to which 0.2 $\mu\text{g/ml}$ BrdU was added 6 hr prior to the end of incubation. Gaps and breaks were examined in 50–100 cells each. After incubation in MEM-FA medium, a chromosome gap was observed at Xq27 at a frequency of 20% in the patient (Fig. 2), and at 1% in his mother. No gaps were observed in his brother or father.

DISCUSSION

DMD is considered to be the most likely diagnosis in this patient based on the age of onset, clinical symptoms, course of illness, and muscle biopsy. Among the diseases to be differentiated, first, congenital muscular dystrophy differs from DMD in the age of onset and involvement of facial muscles. Secondly, malignant limb-girdle type also differs in that it progresses more quickly and is not associated with hypotonia. Thirdly, atypical Fukuyama IV type muscular dystrophy is considered to be excluded, because the time of onset is earlier, and all reported cases of this disease have been females (Ishikawa *et al.*, 1984).

From the above observation, the present patient is considered to have DMD but his clinical profile was different in a number of respects from that of ordinary DMD. First, his mental impairment was severe, secondly, the facial muscles were involved, thirdly, the characteristic thin, long face with large auricles and several minor facial anomalies were present, and fourthly, inherited fragile X was observed. Fragile X denotes a gap or break is present at q27 of X chromosome. If this condition is accompanied by X-linked mental retardation, it is called fragile X syndrome (Wisniewski *et al.*, 1985). The syndrome is considered to be characterized by a retarded motor and verbal development, giant testis, large auricles, protruded forehead and jaw, and restlessness. In this patient, the disease is considered to be X-linked because of the presence of fragile X also in his mother. In addition he had mental retardation and characteristic facial expression. Since giant testis develops after adolescence, all features not consistent with DMD in this particular patient are in agreement with the features of fragile X syndrome.

Therefore, features of both DMD and fragile X syndromes are considered to be admixed in this patient. Wisniewski *et al.* reported that fragile X syndrome was complicated by neurological symptoms, but they were autism and epilepsy (Lubs, 1983). To our knowledge, the concomitant occurrence of muscular dystrophy and fragile X syndrome has not been reported to date. DMD can be readily diagnosed and is seldom accompanied by chromosome aberrations. Therefore, chromosome analysis is considered to be made infrequently in patients with DMD. However, atypical pathology is occasionally encountered in DMD patients. When a peculiar facial expression and minor anomalies suggestive of chromosome aberration are noted as in our patient, chromosome analysis should be carried out.

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