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DUCHENNE MUSCULAR DYSTROPHY IN CHILDREN

Majidova Ya.N., Rashidova Kh.T.
Tashkent State Medical University, Tashkent, Uzbekistan

The diagnosis of Duchenne progressive muscular dystrophy is based on clinical and genealogical history, clinical and biochemical data, electromyography, and pathomorphological examination, which collectively determine the primary myopathic pattern of involvement.

Key words: Duchenne muscular dystrophy, clinical features, diagnostics, children

Relevance. Among the muscular dystrophies, Duchenne, Emery-Dreifuss, and Erb-Roth progressive muscular dystrophies are most frequently diagnosed in childhood [2, 8]. Duchenne muscular dystrophy is a hereditary disease that ranks second worldwide in terms of prevalence (1:5,000 newborn boys) [1, 4]. Duchenne muscular dystrophy is the most devastating of all muscular dystrophies [5].

The genetic factor — a defective gene — is transmitted to the child from the mother, yet the mothers themselves do not develop the disorder. There is a 50 percent chance that each son of a female carrier will develop the disease, and a 50 percent chance that each daughter will become a carrier [3, 6].

Despite nearly a century of study of this pathology, questions regarding its pathogenesis, reliable diagnosis, and treatment remain unresolved to this day. A large number of classification systems exist; however, the absence of precise data on the primary biochemical defect precludes the construction of a classification on a rational basis [1, 7].

Involvement of internal organs considerably aggravates the course of the underlying disease. Patients lose the ability to ambulate independently between the ages of 7 and 13 years and frequently die in adolescence or the third decade of life; virtually all organs and systems of the body become involved in the pathological process [3].

Thus, an analysis of the literature confirms the necessity of conducting thorough somatic examination of patients with progressive muscular dystrophy in order to detect impairments as early as possible and to implement timely corrective measures to maintain the function of vital organs.

In view of the foregoing, the **aim** of the present study was to investigate the clinical and diagnostic features of Duchenne muscular dystrophy in children.

Materials and Methods: A clinical analysis was conducted of 37 children diagnosed with Duchenne progressive muscular dystrophy (PMD). The age of the children ranged from 3 to 15 years, with a mean age of 7.8 ± 0.48 years. The mean age at disease onset was 4.3 ± 0.36 years, ranging from birth to 8 years.

Biochemical investigations included determination of serum enzyme levels: ALT, AST, CPK, and LDH.

Using the genealogical method, 240 first-degree relatives (parents and siblings) of children with PMD were examined. Detailed pedigrees were constructed, incorporating information on diseases

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across three generations of each family. Genealogical data were collected along both parental lines through cross-interviews with both parents and, where applicable, grandparents.

Results and Discussion: Analysis of obstetric history established that pregnancy was complicated by anaemia in 32.4% of cases and by toxicosis in 10.8%. Acute respiratory viral infection during pregnancy was reported by 10.8% of mothers. Exacerbation of chronic conditions during pregnancy was recorded in 2.7% of mothers of affected children. The mean maternal age at birth of a child with PMD was 26.0 ± 0.85 years.

The proportion of family members with PMD was 13.5%.

Based on our findings, PMD cases were identified among full brothers in 4 (10.8%) pedigrees and in one case (2.7%) in a maternal uncle.

Life history data revealed consanguineous marriage in 13.5% of cases. It was also noted that in the majority of cases children were born from the 2nd or 3rd pregnancy (2.2 ± 0.19) or the 2nd–3rd delivery (2.15 ± 0.17).

Two children were from a twin pregnancy; notably, one of the twins was unaffected.

Delivery was normal in 89.2% of cases, precipitate in 5.4%, and prolonged rupture of membranes and operative delivery were each recorded in 1 case (2.7%). Mean birth weight was 3,130 ± 107.3 g. Eight children (21.6%) were born in a state of asphyxia. Umbilical cord entanglement was recorded in 5.4% of children.

Analysis of psychomotor development revealed that in the majority of cases children were late to achieve head control (48.6%) and independent sitting (after 9 months and beyond, 51.3%). Psychomotor development was below age-appropriate norms in 35.1% of cases even prior to the clinical onset of Duchenne muscular dystrophy.

A preliminary diagnosis of PMD was assigned in 78.4% of cases. Of the 37 patients observed, only 1 was under regular follow-up; all others were presenting for the first time.

According to the literature, symptoms typically manifest between 2 and 5 years of age, when the muscles of the lower body and spine are affected first. In our cohort, the first symptoms appeared at a mean age of 4.6 ± 0.35 years.

The principal clinical manifestations of Duchenne muscular dystrophy include: reluctance to walk or slowed gait; abnormal gait, frequently a waddling or swaying pattern; toe-walking; inability to jump or run normally; difficulty ascending stairs or entering and exiting a vehicle; and frequent falls. As a consequence of toe-walking, these children develop anterior pelvic tilt and resultant spinal deformity.

Dental anomalies characterized by mandibular widening and increased interdental spacing were observed in 67.6% of examined children.

Physical examination revealed enlargement of muscle bulk, particularly of the calves; the legs were generally affected symmetrically. Pseudohypertrophy was most frequently observed in children over 6 years of age and tended to diminish as the disease progressed.

Early muscle contractures and retraction of the Achilles tendons developed in 21.6% of the observed children. Muscle atrophy initially localized to the pelvic girdle musculature, with maximal

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severity in the proximal lower extremities, and with advancing age tended to spread in an ascending direction to involve the shoulder girdle, back, and proximal upper extremity muscles.

Detailed neurological examination revealed a waddling gait in 97.3% of cases; active movements were restricted, with difficulty in independent ambulation in 72.9% of cases.

Noteworthy was the reduction and loss of patellar reflexes with relative preservation of Achilles reflexes over an extended period. In older children, diminution of biceps (m. biceps) and triceps (m. triceps) reflexes was observed.

Total muscular hypotonia and reduced muscle strength, more pronounced in the lower extremities, were noted in all cases. Mean muscle strength in the arms was 2.2 ± 0.07 and in the legs 1.25 ± 0.03.

Seizure syndrome was recorded in 2 children (5.4%) and tremor in 1 child (2.7%).

A distinguishing feature of Duchenne muscular dystrophy is the combination of muscle atrophy with pathology of the musculoskeletal, cardiovascular, and neuroendocrine systems.

In the somatic status of the examined children with Duchenne muscular dystrophy, skeletal pathology was prominently expressed in the early stages of the disease. Typical abnormalities included: lumbar hyperlordosis (100%), kyphoscoliosis (94.6%), scoliosis (5.4%), chest deformities of the “keeled” or “scaphoid” type (32.4%), and high-arched foot (100%). As the disease progresses, equinovarus foot deformity and contractures of the large joints develop.

Cardiovascular disorders manifested clinically as pulse and blood pressure lability and muffling of heart sounds. Electrocardiography revealed myocardial changes and bundle branch block.

The most frequent cardiac abnormalities among the examined patients were: pronounced tachycardia, arrhythmias, and development of cardiac failure.

Electrocardiography in patients with Duchenne muscular dystrophy revealed a deep Q wave in leads II, III, aVF, and V6, and a tall R wave in lead V6. These findings are indicative of myocardial involvement in the posteroinferior and lateral walls of the left ventricle.

In patients in the advanced stage of the disease, hypertrophic cardiomyopathy was most commonly identified (51.4%), followed by dilated cardiomyopathy (27%); mitral valve prolapse and left ventricular myxoma were less frequent (21.6%).

Neuroendocrine disturbances were observed in 40.5% of patients; of these, Cushing syndrome was recorded in 53.3% and adiposogenital dystrophy in 46.7%.

Psychomotor skills below age-appropriate norms were observed in 35.1% of examined children, with intellectual disability becoming apparent at an older age.

Electroneuromyographic investigation (ENMG) was performed in 25 of the examined children, comprising recording of biopotentials from the hand and foot muscles, measurement of direct evoked muscle response (M-response) parameters, and late evoked responses (nerve conduction velocity [NCV] and F-wave).

The M-response is an important indicator of neuromuscular apparatus status. In all examined children, this parameter was reduced — both for tibialis anterior on the right (D) and left (S) sides — by approximately 3.5 times compared to the control group ($P < 0.001$). Nerve conduction velocity was

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also significantly lower than control group values bilaterally, measuring 30.6 ± 1.9 and 31.2 ± 2.1 versus 44.8 ± 1.4 and 45.4 ± 1.3, respectively ($P < 0.001$).

Thus, ENMG findings in all examined children demonstrated a primary myopathic pattern of involvement in the proximal lower extremity muscles, with a tendency toward progression and inadequate reinnervation, which became more pronounced with advancing age.

Laboratory parameters were assessed in comparison with those of healthy children (n = 20). This analysis demonstrated that the level of creatine phosphokinase (CPK) in the study group was elevated 71-fold, ALT 15.2-fold, AST 8.4-fold, and LDH 4.4-fold.

Elevated plasma enzyme activity, and particularly elevated CPK, reflects the rate of myofibril degradation within muscle fibres. Concomitant with the rise in CPK, increased concentrations of other cytolysis enzymes — lactate dehydrogenase and transaminases — were observed.

Elevated blood LDH indicates accumulation of blood lactate, which in turn leads to hypoxia, causes a sensation of muscular fatigue, and disrupts the process of cellular respiration.

Elevated transaminase levels (ALT and AST) in the blood invariably indicate a greater-than-normal degree of cell destruction in the corresponding organ — in the present case, the muscles.

Conclusions. The diagnosis of progressive muscular dystrophies constitutes a complex clinical challenge requiring the development and application of diagnostic algorithms. The diagnosis of Duchenne progressive muscular dystrophy is based on clinical and genealogical history and the characteristic clinical features of the disease (onset between 2 and 5 years of age, symmetrical atrophy of proximal muscle groups with ascending progression, pseudohypertrophy of the calf muscles, pronounced somatic and neuroendocrine disturbances, and a rapidly progressive malignant course). Of diagnostic importance are also biochemical findings (serum CPK elevation 71-fold above normal, in conjunction with elevated ALT, AST, and LDH), electromyography, and pathomorphological examination, which collectively establish the primary myopathic pattern of involvement.

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