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A CLINICAL CASE OF CARDIOMYOPATHY IN A PATIENT WITH THE HEREDITARY DISEASE OF PROGRESSIVE ERB-ROTH MUSCULAR DYSTROPHY

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Abstract
Cardiovascular diseases that arise secondarily to neurological disorders are caused either by the direct involvement of the heart in the pathological process or by neurohumoral changes affecting the heart. Cardiovascular involvement developing in patients with neurological pathology is sometimes associated with a higher risk of morbidity and mortality than the primary neurological disorder itself (Braunwald).

Keywords: Myopathy, lumbar-limb muscular dystrophy, cardiomyopathy, myopathy erb-roth, limb-girdle muscular dystrophy, cardiomyopathy.

Introduction

It is now well-established that most progressive muscular dystrophies are accompanied by the development of cardiomyopathy (Finsterer J., Stöllberger C., 2008; Groh W.J., 2012; Van Spaendonck-Zwarts K.Y. et al., 2013). Developing as early as childhood, cardiomyopathy and associated cardiovascular disorders are a leading cause of death in patients with progressive muscular dystrophies (Van Bockel E.A., 2009; Neuen-Jacob E., 2009; Fayssoil A., 2010).

Progressive muscular dystrophies constitute a heterogeneous group of severe genetically determined disorders characterized by damage to muscle structures, leading to disability and fatal outcomes (Badalyan L.O. et al., Ilyina N.A., Badalyan L.O., Grinio L.P., Agafonov B.V., 1997; Veltiscev Yu.E., Temin P.A., 1998). Over the past decade, there has been a significant increase in research focusing on the molecular-genetic aspects of muscular dystrophies. However, researchers have primarily focused on the relationship between genetic defects and skeletal muscle damage, paying comparatively less attention to cardiovascular involvement, the genesis of cardiac decompensation, and the potential for correcting these abnormalities.

Muscular dystrophies involving the cardiovascular system are classified as follows:

1. Duchenne and Becker muscular dystrophies
2. Myotonic dystrophies
3. Emery-Dreifuss muscular dystrophy and associated disorders
4. Limb-girdle muscular dystrophies
5. Facioscapulohumeral muscular dystrophy

Limb-girdle muscular dystrophy (LGMD), including Erb-Roth myodystrophies, is a group of polymorphic and genetically heterogeneous disorders characterized by predominant involvement of the pelvic and shoulder girdle muscles. The prevalence of all forms of LGMD varies across populations, ranging from 5 to 70 cases per 1 million people [1]. Over 20 genetic variants of LGMD have been described, divided into two subgroups based on inheritance type: LGMD type 1 with autosomal dominant inheritance and LGMD type 2 with autosomal recessive inheritance. Erb-Roth myopathy belongs to the second group. The first report of an autosomal recessive variant of LGMD was published in 1895 by physician W.K. Roth, who described a specific phenotype in a 22-year-old patient [2].In autosomal recessive inheritance (accounting for 85–90% of cases), the production of sarcoglycans - proteins that are part of the plasma membrane—is typically disrupted. Autosomal dominant forms of muscular dystrophy result from defects in the synthesis of membrane proteins, sarcomeric proteins, and nuclear proteins. Symptoms develop gradually, and the age of onset is not always easily determined. In the autosomal recessive variant, symptoms usually appear at 14–16 years of age, though they may occur earlier, between 5 and 10 years. In the autosomal dominant variant, onset typically occurs between 20 and 25 years.

Characteristic symptoms include muscle weakness, pathological muscle fatigue with physical activity, and gait abnormalities such as a "waddling" or "lordly" gait. Early in the disease, atrophy is localized in the proximal muscle groups of the lower limbs, and in later stages, it progresses to involve the back, abdominal, and distal limb muscles. In some cases, both pelvic and shoulder girdle muscles are affected simultaneously. As atrophies progress, hyperlordosis, "winged" scapulae, a "wasp-like" waist, and "hollow" shoulders may develop. Patients often use compensatory techniques to rise from a seated position. Pseudohypertrophy of muscles, joint contractures, and tendon retractions are generally moderate. Knee reflexes and reflexes of the biceps and triceps brachii are typically reduced. Cardiomyopathy may also develop.

The involvement of the heart muscle and conduction system in Erb-Roth muscular dystrophy is particularly critical, as it is the leading cause of death in these patients [4]. An example of cardiac muscle and conduction system involvement in Erb-Roth muscular dystrophy is the case of patient E., a 19-year-old male. He was admitted to the neurology department with complaints of pronounced muscle weakness in his arms and legs, a "waddling" gait, general weakness, inability to run, difficulty rising from a seated position, and trouble climbing stairs.

History of the present illness: The patient is the only child in a family where the parents are not related. The onset of LGMD symptoms occurred around the age of 13, when noticeable weakness in the pelvic girdle and thigh muscles first appeared (the patient experienced difficulties meeting physical education requirements, particularly in squatting, running, etc.). The disease progressed gradually but steadily. Difficulties climbing 1–2 flights of stairs arose, and significant muscle hypotrophy of the thighs and pelvic girdle developed. His gait changed, and over the next two years, he experienced atrophy and weakness in the distal muscles of the limbs, shoulders, and scapular regions. The gait became more pronouncedly waddling, accompanied by hypermobility in the hip joints, muscle pain in the lower back, and the development of thoracolumbar scoliosis.

The patient has undergone multiple hospital treatments and has been under regular observation by a neurologist.

Upon physical examination, the patient's condition is stable, with a passive and forced posture. Atrophy is noted in the proximal and distal muscle groups of the lower limbs, as well as the back, abdominal, and shoulder girdle muscles. The patient exhibits hyperlordosis, "winged" scapula, and "hollow" shoulders. When rising, the patient uses compensatory maneuvers. The skin is pale and clean. Percussion of the lungs reveals pulmonary resonance; auscultation indicates diminished vesicular breath sounds. Respiratory rate: 16 breaths per minute. The cardiac borders are not enlarged; heart sounds are muffled but rhythmic, with a systolic murmur at the apex and accentuation of the second tone over the pulmonary artery. Heart rate and pulse: 105 beats per minute. Blood pressure: 110/80 mmHg. The tongue is moist and coated. The abdomen is nontender upon palpation. The liver and spleen are not enlarged. Bowel movements tend toward constipation, with no dysuria or peripheral edema observed. Psychoneurological status: The patient's condition is of moderate severity. Consciousness is clear; the patient is oriented and communicative. Intellectual function corresponds to age and education level. Cranial nerves: No olfactory disturbances are present. Pupillary light reflexes (direct and consensual) are brisk on both sides. Full range of eye movement is present without diplopia, anopsia, amaurosis, or amblyopia. No anisocoria or nystagmus is observed. Sensory disturbances in the face are absent. There is mild weakness of the masticatory muscles, with a muscle strength score of 5/5. A slight diparesis of the facial nerve is noted, with a positive "eyelash" sign on both sides. No bulbar dysfunction is evident (speech, phonation, and swallowing are clinically normal).Motor function: Proximal peripheral tetraparesis is present. Diffuse muscle hypotrophy is pronounced in the proximal muscles of the shoulder and pelvic girdles, accompanied by thoracolumbar scoliosis, a "myopathic" abdomen due to weakness and hypotrophy of the abdominal oblique muscles, and lumbar-sacral hyperlordosis. Muscle tone is diffusely and moderately reduced, predominantly in the proximal regions of the upper and lower limbs (thighs and shoulders), with no side asymmetry. Hypermobile large joints in both the upper and lower extremities are noted due to muscle hypotrophy. Muscle strength is reduced to 1/5 in the proximal regions of the upper and lower limbs and to 5/5 in the distal regions, with no asymmetry. When rising from a supine position on the couch to a standing position, the patient uses compensatory maneuvers characteristic of the "Gowers' sign."Tendon reflexes are absent in both the upper and lower limbs, indicating tetra-areflexia.

The gait is a "waddling" type, unstable, with pelvic rocking and frequent stumbling. There are no coordination or sensory disturbances. Sensory function: No abnormalities in superficial or deep sensitivity were detected. Pelvic organ function: Constipation, attributed to significant hypotrophy and weakness of the anterior abdominal wall muscles, is chronic, habitual, and hypotonic. Laboratory findings upon admission: Complete blood count: leukocytes 4.6×10^9/L, hemoglobin 94 g/L, erythrocyte sedimentation rate (ESR) 18 mm/h; otherwise unremarkable. Elevated C-reactive protein (CRP) at 96.0 mg/L. Urinalysis:proteinuria at 0.099 g/L.Blood biochemistry: within normal limits. Electrocardiography (ECG):Sinus tachycardia with a heart rate of 120 beats per minute. Vertical electrical axis of the heart. Hypoxic changes in the myocardium.Intraventricular conduction disturbances and incomplete right bundle branch block. Echocardiography:Heart chambers: normal shape, size, and proportions. Ejection fraction: 78%.Overall myocardial contractility: preserved.Heart valves: no abnormalities in structure or kinetics. Diastolic dysfunction of the left ventricle (grade II).Mitral and tricuspid valve insufficiency (grades 2–3).Pulmonary hypertension.

This case of Erb-Roth myopathy represents a congenital pathology with pronounced clinical manifestations. In this type of myopathy, not only the striated skeletal muscles are affected but also the cardiac muscle. Limb-girdle muscular dystrophy type 2A is characterized by myocardial remodeling due to secondary factors (valvular dysfunction) in the absence of cardiomyopathy or systolic myocardial dysfunction. Erb-Roth myopathy must be differentiated from other muscular dystrophies, such as Duchenne muscular dystrophy, Emery-Dreifuss dystrophy, Becker dystrophy, dermatomyositis, polymyositis, amyotrophic lateral sclerosis, toxic myopathy, and others. Specific forms:Emery-Dreifuss muscular dystrophy (X-linked and autosomal dominant forms): Associated with arrhythmogenic cardiomyopathy, atriomegaly, predominant rhythm and conduction disturbances, and a high risk of sudden cardiac death. Duchenne and Becker dystrophinopathies: Characterized by cardiomyopathy with early heart failure and potential myocardial ischemia presenting as angina syndrome, as well as arrhythmic disturbances, particularly in Becker muscular dystrophy.

Heart involvement in progressive muscular dystrophies (according to Groznova O.S., 2013):Myocardial variant: seen in Duchenne muscular dystrophy. Arrhythmogenic variant: observed in autosomal dominant Emery-Dreifuss dystrophy. Valvular variant: characteristic of limb-girdle muscular dystrophy type 2A.Mixed variant: noted in Becker dystrophy and X-linked Emery-Dreifuss dystrophy.

According to global standards for echocardiographic research, six clinical and pathogenetic stages of cardiovascular system involvement in neuromuscular diseases are distinguished [Quinlivan-RM; Dubowitz-V, 1992]:

1. Diastolic dysfunction of the myocardium with a restrictive pattern at the early stages of the disease: This includes a decrease in blood flow velocity at the mitral valve, with reduced amplitude of the atrial wave, decreased diastolic diameter and volume of the left ventricle, and a moderate reduction in the left ventricular ejection fraction.
2. Myocardial stabilization at the compensation stage of the disease: Normalization of Doppler echocardiographic parameters. At these stages, it is advisable to use cardiotropic therapy orally 2–3 times a year (ATP-long, riboxin, mildronate, cardonat, elcar, potassium orotate, magnerot).
3. Systolic dysfunction of the myocardium at the subcompensation stage of the myopathic process: This includes moderate enlargement of the left ventricular systolic diameter and volume, along with a moderate decrease in the ejection fraction.
4. Myocardial pseudostabilization at the decompensation-A stage of the myopathic process: Normalization of Doppler echocardiographic parameters.
5. Hypokinesia of the left ventricle at the decompensation-B stage: Significant increase in the systolic diameter and volume of the left ventricle, along with a significant reduction in the ejection fraction.
6. Left ventricular dilation at the decompensation-C stage: Significant enlargement of both the diastolic and systolic diameters and volumes of the left ventricle, with a sharp reduction in the ejection fraction [edited by V.K. Widerhold, 2004].

The use of calculated echocardiographic parameters allows for a more detailed understanding of the pathogenesis of the disease, identifies pre-pathological changes, and enables early treatment initiation. This approach helps extend the period of independent walking for patients and delays the onset of manifest heart failure [edited by V.K. Widerhold, 2004].

Thus, cardiomyopathy in PMD (progressive muscular dystrophy) in children develops against the backdrop of patient hypoactivity, which is why heart failure of stages I and II does not manifest on time, and life-threatening arrhythmias and conduction disorders do not provoke clinical symptoms, leading to late diagnosis of cardiovascular disorders and fatalities. Management of patients with the above-mentioned diseases is carried out according to the algorithm for diagnosing cardiovascular disorders. The first step is performing an ECG to detect rhythm, conduction, and repolarization abnormalities in the myocardium. The second step involves differentiated examination: if repolarization abnormalities are found, echocardiography is performed to detect myocardial remodeling and myocardial dysfunction; if rhythm and conduction abnormalities are detected, Holter monitoring is used to clarify the nature of the disturbances, and echocardiography is done to detect arrhythmic myocardial abnormalities. The third step involves prescribing differentiated therapy and determining the indications for surgical treatment (radiofrequency ablation, implantation of a cardioverter-defibrillator, or pacemaker).

Cardiotropic treatment for patients with progressive muscular dystrophies should begin before the clinical signs of heart failure and/or the clinical manifestations of rhythm and conduction disorders occur, as after the onset of clinical symptoms, the treatment's effectiveness is low, and the likelihood of life-threatening conditions is high. The required frequency of patient monitoring ranges from once every 3 months to once a year, depending on the detected changes. In the absence of cardiovascular disorders, patients with PMD should undergo repeat examinations according to the algorithm once a year. If changes are detected, medication therapy should be initiated before signs of circulatory failure appear and before clinical manifestations of rhythm and conduction disorders emerge.

It has been shown that the treatment of cardiomyopathy and accompanying cardiovascular disorders in patients with progressive muscular dystrophies should be based on clinical presentation and genetic confirmation of the diagnosis, as this allows for the prediction of the development of cardiomyopathy in the patient, the timing of its onset, the course of the disease, clinical manifestations, and outcome. Treatment of cardiomyopathy and associated cardiovascular disorders in PMD is carried out before the development of heart failure symptoms (with angiotensin-converting enzyme inhibitors, beta-blockers, and low-dose prednisone) and/or clinical manifestations of rhythm and conduction disorders (antiarrhythmic drugs or implantation of a monocentric pacemaker), which reliably leads to increased survival in patients (Groznova G., 2013).

The problem of cardiovascular involvement in neuromuscular diseases is relevant because the fatal outcome in most of these conditions is caused precisely by the involvement of the heart in the pathological process, as the heart muscle is primarily affected due to the deficiency of the same structural component that is also absent in skeletal muscle. The heart is a continuously and intensively working organ, and often the onset of myopathy begins with cardiological manifestations, while the symptoms of the myopathic process may be masked [Strakhova O.S., Belozerova Y.M., Temin P.A., 1999].