CONNECTIVE TISSUE DYSPLASIA IN CONTEXT OF SPORT TRAININGS, PHYSIOTHERAPY AND SPORTS HEALTHCARE

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Key words: connective tissue dysplasia, marfanoid phenotype, muscle mass, thyroid gland, sex, autoimmune thyroiditis, sport, physiotherapy.

Introduction. Human musculoskeletal system is a tool of his physical, in particular sport, activity - consists entirely of mesenchymal derivatives. Connective tissue dysplasia (CTD) is a group of its systemic diseases of genetically determined, mono- or polygenic multifactorial nature, stipulated by the impaired development of mesenchymal derivatives in the embryonic and postnatal periods, and is characterized by self-assembly tissue defects on the basis of its anomalies of recognizing it proteins or bio-regulators and their receptors [8]. The most common mild forms of CTD combined with undiagnosed primary genetic defects may be interpreted as a constitutionally determined prenosological diathesis, which in terms of an unfavorable course or effects of risk-factors might lead to failure of adaptation mechanisms resulting in a disease. CTD is combined into syndromes and phenotypes. Differentiated (syndromic) CTD is a group of hereditary monogenic diseases characterized by a certain mode of inheritance, clear disease patterns, and, most commonly, by identified and thoroughly studied genetic or biochemical defects. Among these are: Marfan syndrome, Chernogubov-Ehlers-Danlos syndrome, brittle bone syndrome, Stickler syndrome, Wagner syndrome, etc. Undifferentiated (nonsyndromic) CTD (UCTD) is a genetically heterogeneous group of polygenic, epigenetic-dependent forms that do not fully fit under the pattern of particular monogenic syndromes and are associated with a number of chronic diseases. In fact, UCTD come as nonstrictly determined, overlapping in symptoms and signs copies of the familiar syndromes. Among them are: marfanoid, Ehlers-like phenotypes, as well as unclassified phenotype. Chernogubov-Ehlers-Danlos syndrome and the Ehlers-like phenotype (EP) may come amid the development of joint hypermobility, particularly - under the tenascin-X mutation. Mutations in the fibrillin gene (fibrillinopathy), and anomalies of crossing-over of the transforming growth factor-β and its receptor are responsible for development of Marfan syndrome and the marfanoid phenotype (MP) [2].

Relevance. Monogenic syndromes of CTD are rare, however, the frequency of UCTD in Russia ranges from 8.5% to 80% depending on the region and population [8]. Carriers of these genetic abnormalities are characterized by strongly-marked peculiarities of the structure and functions of their locomotor system, which actualize the problem of CTD for sports medicine and sports healthcare. Thus, morphologically such individuals are diagnosed with the loss of muscle fibers in skeletal, cardiac and oculomotor muscles, which is accompanied by a decrease in the myocardial contractility and often by the development of myopia and amblyopia. This leads to muscle hypotonia and impaired posture in patients from early childhood, and as they move through adolescence some kind of myasthenic syndrome with the signs of a high-grade musculoskeletal dysplasia develops in them. At the same time, most individuals with CTD due to hyperflexibility (double-jointness) and psychophysical characteristics (for instance, a disposition to ambidexterity and high capacity for work) are prone to dancing (ballet dancers), and sport (figure skating, rhythmic gymnastics, acrobatics, fencing, track and field athletics, swimming and diving, volleyball, football, multi-sport events); with that, they often achieve a standout success in their activity. Thus, it is known that most Olympic champions in gymnastics, swimming and figure skating are diagnosed with CTD [3, 4]. Moreover, physical loads are rather dangerous when it comes to CTD. There are known cases of a sudden death from the rupture of vascular aneurisms which are typical for MP among Olympic medalists-marfanoids (volleyball player Flora Jean Hyman (1954-1986), track and field athlete and multiathlonist Liesel Prokop-Sykora (1941-2006) and others). In case of EP, decreased proprioceptive sensitivity and increased pain sensitivity have been proven. In case of CTD, there is an increased risk of injury, and there often develops fibromyalgia or the chronic fatigue syndrome. Thus, the joint hypermobility syndrome in Ukrainian teenage football players was diagnosed more often than population mean - more than in one third of the studies and was determined by the low recoverability of an organism after loads [5]. On the other hand, physiotherapy tools are successfully used for the purpose of health improvement in such adolescents, since fibromyalgia decreases due to exercises. Consequently, individuals with MP, especially youngsters whose phenotype development has not finished yet, are a major focus of interest for specialists in the sphere of sports medicine, physiotherapy and sports healthcare.

The purpose of the study was to establish the relationship of muscle mass, thyroid function (TF) and the features of the marfanoid phenotype (MP) in male and female individuals of different ages.

Materials and methods. We examined a total of 757 individuals with the signs of MP identified by the Ghent criteria [2] (570 - females) aged 14-63 years, adolescents among them (up to 21 year) - 195. Clinical and laboratory methods were applied, including enzyme immunodetection of thyroid hormones - thyroxine (T4), triiodothyronine (T3), thyroid-stimulating hormone (TSH),

cortisol (CS), thyroglobulin antibodies (TgAb) and thyroid peroxidase antibodies (TPOAb), thyroid ultrasonography (US). Anthropometrically, in order to evaluate the intensity of MP we measured height, body length and lower limb length and calculated the dolichostenomelic index (DI+(height-LL length)/LL length) [2]. Muscle mass (MM) of individuals was calculated using the Dupe-Martin Lee formula [3] as follows below (BM - body mass, L - height): MM = 0,244 × BM (kg) + 7,8 × L (m) + 6,6 × sex – 0,098 × age (years) + race – 3,3. The data were processed using the parametric methods of variation statistics and the Student-Fisher t-test.

Results and discussion. According to our study, adolescents with the diencephalic syndrome (DS) have a number of characteristic features typical for MP, at the increased CS level (839,9±30.4 nM/l) which has a catabolic effect on muscles. Large majority of these youngsters were determined to have anti-thyroid autoantibodies and autoimmune thyroiditis (AIT) [7, 10]. It is known that thyroid hormones stimulate both biosynthesis and degradation of protein in skeletal muscles, where in case of thyrotoxicosis, it is catabolic effects that prevail in them, and in case of hypothyroidism - it is a slowdown of protein biosynthesis [8]. Taking account of these endocrine effects on MM, we were able to trace the relationship between MM and thyroid hormones in blood in 73 teenage draftees with DS (mean age - 17,5±0,1 years; mean BM – 105,5 kg). In theory, when it comes to the primary (alimentary-constitutional) obesity developing without hypercorticism, MM should be greater than in case of DS. In order to prove this hypothesis we examined 73 teenage draftees of the same age (17,6±0,1 years; mean BM – 95,6 kg) but with the primary (alimentary-constitutional) obesity and normal CS level in blood (619.3±27.2 nM/l). MM in adolescents with the primary obesity was significantly greater than in obese adolescents with DS, while their BM was on the average 10 kg less. As the teenage groups were ideally comparable in sex and age, there are grounds for crediting the Dupe-Martin Lee formula when determining MM of an individual [1]. Next, we examined 120 patients (100 females) suffering from AIT aged 25-60 years (mean age – 34±0,6 years) with different BM. The changes in the thyroid functions were supplemented by certain fluctuations of MM, however, the relationship between T_4 and MM in males and females was different. With raising MM, T_4 concentration in the blood stream increased in females but decreased in males. At the same time, loss of MM in females was accompanied by the reduction of T_4 in blood, while in males, on the contrary, it increased. MM fluctuations in the examined males and females hardly depended on the hypothyroidism compensation ratio, since MM varied multidirectionally in heterosexual patients with similar AIT compensation ratio [1]. In children and youngsters with UCTD, AIT was observed 3 times as often as without one, and as a rule, in the setting of the predisposing juvenile thyroid hyperplasia. We studied the thyroid function in 195 teenage draftees with hypotrophy and different signs of MP to discover the tendencies to the increase in the level of T_3 (up to 2,25±0,06 against 1,74±0,06 nM/l in the control group), the

decrease of T_4 (107,6±0,1 against 124,4±3,3) and the increase of TSH (2,14±0,13 against 0,99±0,06 mcU/ml). Autoantibodies to the thyroid gland were registered in 11.5% of the examined. US allowed to determine an echogenic pattern, AIT in a half of the adolescents: hypoechogenic and unhomogeneous pattern, cysts and nodules. In case of MP, 100% of adolescents were determined to have TgAb (11,1±3,45 mU/ml) and TPOAb (0,95±0,06), the intensity of the signs of AIT correlated to CTD [4, 6, 9].

We also examined 194 individuals aged 14 to 50 years (170 females) with MP and estimated their thyroid gland functional status and characteristics of their immunoendocrine reactivity. In the general group of the examined the level of T_3 equaled 1,71±0,3 nM/l, T_4 – 96,9±17,2 nM/l, TSH – 1,9±0,3 mcU/ml, TgAb – 94,4±47,7 U/ml, TPOAb – 86,4±42,4 U/ml; and in healthy individuals T_3 – 2,09±0,04, T_4 – 114,3±1,6, TSH – 2,06 ± 0,05, Ab to the thyroid gland were not found. In the experimental group consisting of 40 individuals with pronounced hypothyroidism these indicators were as follows: T_3 – 1,93±0,38, T_4 – 85,52±6,42, TSH – 5,24±1,5, TgAb – 87,3±36,4, TPOAb – 505,7±180. With aging, individuals with MP clearly display an increasing decline in the production of T_3 and T_4 and a rise in the level of TSH and antibodies to the thyroid gland, which by US was seen as the thyroid volume increase [4, 9]. It can be expected that MP leads to a risk of the regular development of AIT resulting in hypothyroidism [10]. It is knows that in case of MP, height in a sitting posture always, to a greater or lesser degree, exceeds lower limb length (LL<0,89) [2]. With that, this disproportion increases with the increasing height of patients. Taking into account the high frequency of AIT at MP we tried to determine the relationship between MM and T_4 level and the intensity of the marfanoid features in individuals with AIT, so we examined a total of 370 patients with MP and AIT (300 - females) aged 24-63 years (mean age 34±0,6 years). In individuals with AIT and MP lower limb shortening was supplemented by the loss of MM: the more pronounced MP was, the more MM was affected. In the meantime, the loss of MM is accompanied by the increase in the level of T_4 in males, and its decrease in females. Thyroid hormones promote the biosynthesis of sex steroids in both genders. However, by stimulating the synthesis of muscle protein they also come as antagonists to the anabolic action of testosterone. As opposed to androgens, estrogens do not have any significant effect on human muscle mass [11], which is implicitly proved by over studies. This is why there was determined an inverse relationship between the level of T_4 and MM in males with AIT and their close relationship in females with AIT.

Conclusions: Young athletes with the marfanoid phenotype prone to autoimmune thyroiditis should be considered at high risk. Normalization of thyroid function in athletes may provide the basis for increasing their athletic potential and longevity in sport. At the same time, thyroid hormones in any way can not be equated to doping for such individuals in need of prevention and treatment of autoimmune thyroiditis, the marfanoid phenotype predisposes them to

it [10]. Since aging is accompanied by the correlative decrease in muscle mass, thyroid hormone level and certain indicators of immunity [12] and, according to the researchers' data [8], is greatly accelerated with decompensated autoimmune thyroiditis, the presented results may indicate the value of using the Dupe-Martin Lee formula and determination of thyroid status not only in sports medicine, but also when estimating the real biological age of an individual.

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