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DEBATABLE QUESTIONS ABOUT THE PATHOLOGICAL COURSE OF PREGNANCY AND CHILDBIRTH IN CONNECTIVE TISSUE DYSPLASIA

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ABOUT ARTICLE

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Abstract: The main function of connective tissues is to provide structural support to other tissues. Cartilage and bone are the main connective tissue types, other types are areolar connective tissue, which holds organs together, and dense connective tissue, which forms ligaments and tendons. We studied 47 pregnant women with uBD and 15 healthy pregnant women without uBD aged 24 to 30 years. 50% of women with uBD were at risk of abortion, and the risk of preterm birth was observed 6 times more often than in healthy pregnant women. Thus, pregnant women with signs of various forms of uBD belong to high-risk groups for obstetric and perinatal pathology and therefore need to be closely monitored during pregnancy, childbirth and the postpartum period. In addition, newborns who have a high probability of inheriting this disease must be examined.

INTRODUCTION

Undifferentiated connective tissue dysplasia (UCTD) is a group of genetic disorders that affect the body's connective tissue. Connective tissue provides support and structure to many parts of the body, including bones, joints, skin, blood vessels, and internal organs. In UCTD, connective tissue is weak and deformed, which can lead to a wide range of health problems.

Symptoms of UCTD can vary from person to person, but may include:

- Joint hypermobility: Joints may be loose and dislocate or sprain easily.

- Joint and muscle pain: Pain can be dull or aching and may worsen with activity.
- Muscle weakness: Muscles may be weak and tire more easily than usual.
- Skin problems: Skin may be stretchy, loose, or bruise easily.
- Cardiovascular problems: There may be problems with the heart valves or the aorta (the main artery leaving the heart).
- Lung problems: There may be difficulty breathing or a risk of pneumothorax (collapsed lung).
- Digestive problems: There may be problems with digestion or hernias.

Diagnosis of UCTD is typically based on the person's medical history, physical exam, and various tests, such as X-rays, ultrasounds, and genetic tests.

Treatment of UCTD depends on the person's specific symptoms. There is no cure for UCTD, but treatment can help improve symptoms and quality of life. Treatment may include:

- Physical therapy: Exercise can help strengthen muscles and improve range of motion.
- Orthotics: Orthotics, such as braces or splints, can help support joints and reduce pain.
- Medications: Medications can be used to relieve pain, inflammation, and other symptoms.
- Surgery: Surgery may be necessary to correct serious problems, such as a dislocated joint or heart problems.

The prognosis for people with UCTD varies depending on the severity of their condition. With proper treatment, most people with UCTD can lead normal and productive lives.

The main function of connective tissue is to provide structural support to other tissues. Cartilage and bone are the most important connective tissue types, other types are areolar connective tissue, which holds organs together, and dense connective tissue, which forms ligaments and tendons. Undifferentiated connective tissue dysplasia is a heterogeneous group of diseases that can lead to various chronic diseases. uBD often corresponds to abnormal structural and functional changes in connective tissue. This leads to disorders of the morphology and function of organs [11]. The clinical and morphological manifestations of uBD are extremely diverse. These can include skeletal changes associated with cartilage diseases, disproportionately long limbs, arachnodactyly, breast deformities, spinal scoliosis, flat feet, pathology of tooth development, occlusion, cysts, joint pathology (tendency to dislocation), hyperelasticity, thinning, a tendency to traumatize the skin, varicose veins and external signs of accelerated aging - early wrinkling, deformation of the facial oval, including gravitational ptosis (Sagging of the soft tissues of the face) [8,9]. Lesions of the cardiovascular system are very diverse: mitral valve prolapse (the most common of all heart abnormalities in connective tissue is usually

detected by echocardiography), venous insufficiency, varicose veins and hemostasis pathologies [7]. The diagnosis of uBT is based on these symptoms and additional findings (e.g., anthropometry, external breathing, reduced heart size, low blood pressure, plethysmography, specific features of ECG, and ultrasound phleboscan) [10]. According to the analysis of these phenotypic markers of uBT, its prevalence in the general population may be relatively high (e.g., 8.5% in a sample of 400 individuals [9]). Although it is often claimed that the etiology of BT has a genetic component, no comprehensive analysis of the relative roles of environmental factors (diet, environmental conditions, exercise hygiene, psycho-emotional background) and genetic factors has been conducted. The term "dysplasia" refers to the abnormal growth/development of a tissue or organ. The diagnosis of BT is made on the basis of a thorough analysis of symptoms and the results of clinical trials. However, the diagnosis of BD is rarely accompanied by specific histological confirmations in practice. Accordingly, clinically proven dysplasia can correspond to numerous changes in the tissue structure.

In connective tissue, dysplasia (i.e., "abnormal growth") can occur due to: 1) abnormal collagen synthesis or composition; 2) Synthesis of abnormal collagen; 3) excessive collagen breakdown; 4) Disorders of the structure of collagen fibers due to insufficient cross-linking; 5) similar abnormalities associated with elastin fibers; 6) Tissue destruction due to autoimmune reactions [5,7]. According to Y. Chia, mitral valve prolapse accounts for 60.8% of congenital heart disease in pregnant women [3]. The clinical polymorphism of mitral valve prolapse is often accompanied by other signs of connective tissue dysplasia: asthenic physique, pathological joint mobility, myopia, flat feet as well as prolapse of other heart valves, open foramen ovale, nephroptosis, biliary dyskinesia, varicose veins and increased bleeding. It is known that additional pathways are found 3 times more often in patients with mitral valve prolapse than in the general population [2].

Most often, mitral valve prolapse is asymptomatic and has a favorable prognosis, but is sometimes associated with cardiac arrhythmias, heart failure, thromboembolism, infectious endocarditis, and sudden death. The peculiarities of hemodynamics of the gestational period, namely an increase in circulating blood volume and cardiac output, increase the load on the cardiovascular system and can provoke the development of these complications. In some cases, women with mitral valve prolapse experience signs of heart failure and paroxysmal arrhythmias during pregnancy [6]. The greatest threat is posed by patients with hemodynamically significant mitral regurgitation and myxomatous degeneration of the valve leaflets, which are the source of blood clots and the cause of thromboembolic complications [12].

In recent years, the problem of pregnancy and childbirth in women with uBD, a genetic disorder of their development in the embryonic and postnatal periods, has been actively discussed. As a result of various mutations in the genes that encode the structure of collagen and elastin, defects form in the fibrous structures and the main substance of uBD, followed by the development of various morphofunctional disorders of a systemic and local nature [6]. The morphological basis of uBD is a decrease in the content of certain types of collagen or a violation of the ratio between them, which leads to a decrease in the strength of the connective tissue of many organs and systems. The outward manifestation of uBD is the so-called "dysembryogenesis stigmata", which can manifest as both obvious deformities and subtle signs. Up to 35% of healthy people have some degree of uBD, and 70% of these are women [3]. The variety of mutagenic effects on the development of this pathology determines a wide range of its clinical variants – from known gene-differentiated syndromes (Marfan, Ehlers-Danlos) – to numerous hereditary undifferentiated (non-syndromic) uBDs. uBD are considered "phenotypic" copies of known syndromes [8]. The generalized nature of connective tissue damage affects the pathological development of the organs of the reproductive system, which in turn provokes the manifestation of a number of obstetric problems [12]. In contrast to syndromic forms, uBD manifests itself mainly through mild heterogeneous symptoms and syndromes, which are summarized under the general name "dysembryogenesis stigmata" [1,3]. The specifics of pregnancy and childbirth in women with uBD have not been sufficiently studied and are the subject of the researchers' attentive attention. Women with uBD are significantly more likely to experience pregnancy pathologies than healthy women – 85.5% versus 53.3%. In the literature, there is evidence of a higher incidence of the risk of early and late abortion in women with uBD. There is also a higher incidence of preeclampsia and eclampsia in women with uBD [7,8].

MATERIALS AND METHODS

We studied 47 pregnant women with uBD and 15 healthy pregnant women without uBD aged 24 to 30 years. 50% of women with uBD were at risk of abortion, and the risk of preterm birth was observed 6 times more often than healthy pregnant women. The main cause of recurrent miscarriage in this patient group was isthmic-cervical insufficiency. At the same time, according to our data, in almost 1/3 of the cases, there was a risk of abortion in a period of up to 20 weeks, the risk of premature birth - in 17.2%, the pregnancy ended in premature birth in 4.6% of cases. Analysis of the course of the pregnancy process in pregnant women with uBD showed that one of the most common complications was early gestosis, which occurred in 48.6% of cases. At the same time, there was a direct significant correlation between the severity of the clinical picture and the frequency of early gestosis. According to our data,

preeclampsia was the most common complication in the second half of pregnancy in women with uBD (49.8%), and the birth process in these patients was characterized by frequent complications. It is known that preeclampsia occupies the 2nd-3rd place in the structure of causes of maternal mortality and is one of the main causes of premature birth and perinatal fetal death. One in five children of a mother with preeclampsia has some degree of abnormalities in physical and psycho-emotional development. Placental dysfunction was also very common in uBD – in 37.5% of cases. At the same time, there was a violation of uteroplacental and fetal hemodynamics, transport, trophic, endocrine and metabolic functions of the placenta, which led to fetal malformations (12.1%).

However, this assumption cannot be considered indisputable. The main clinical manifestation of placental dysfunction in pregnant women with uBD was fetal distress. Microscopy of the placenta in puerperas with uBD showed various forms of impaired placental maturation. Another, no less important complication for obstetrics - untimely discharge of amniotic fluid - was observed in 40.0% of cases in women with uBD. The incidence of premature and early rupture of amniotic fluid in our pregnant women with uBD ranged from 37.4% to 41.7% of cases. The microscopic picture of fetal membranes in uBD was characterized by thickening of the compact layer of the amnion of varying degrees of severity due to the proliferation of collagen fibers in it. Of the features of the course of labor associated with uBD, a relationship with a rapid and rapid course of labor was revealed, and in severe cases of uBD, the frequency of rapid and rapid labor in primiparous women reached 47%, and in mild signs of uBD was about 14%. Recently, a new concept of the development of labor weakness (DLW) has been put forward, in which its causal factor may belong to the uBD. The data of the literature review indicate a fairly high incidence of ECS, which is 2-10% in parturient women with its primary development and 2.5% in its secondary development. In women over 30 years of age, ECS is 2 times more common than in women aged 20-25 years. ECS leads to a protracted course or complete cessation of labor, the appearance of signs of fetal distress, which leads to prompt delivery. In the structure of emergency caesarean section, ECS ranks 2-3rd, reaching 37% [9,10]. It is known that during pregnancy there are significant changes in the structure of muscle tissue and collagen fibers of the cervix. The volume of muscle tissue increases by more than 2 times due to the growth of the vascular link with the simultaneous destruction of collagen fibers. In the course of many studies, it was found that in 15-20% of women such changes were not observed, which made it possible to attribute such patients to the risk group for the development of abnormalities in labor [14]. Another discussed cause of DRD is the pathology of immune status. As is known, endogenous prostaglandins and endothelial growth factors play an important role in the nature of labor [13]. It has been established that the main role in the development of labor belongs to the fetus. At the junction of maternal and fetal tissues in the uterus,

there is a release of the main modulators of myometrial contractile activity - prostaglandins of fetal and maternal origin. As a result, another mechanism of childbirth is triggered - immunological rejection of the fetus [10]. Cytokines such as interleukin-1 (IL-1), IL-6, IL-8 and tumor necrosis factor (TNF-) are of great importance in the mechanism of labor [11]. The study of the peculiarities of the course of pregnancy and childbirth in 47 patients with small and large signs of uBD made it possible to establish that abnormalities of labor in the first stage of labor occurred in 75.3% of parturient women against 23.7% in the control group without uBD. Caesarean section in the study group was performed in 15% of pregnant women and only in 3% of patients in the control group. Hypotonic bleeding in the third stage of labor occurred in 7.8% of mothers with uBD and was absent in the control group. Pubic joint divergence was diagnosed in 8.3% of women with uBD and was not detected in the control group. Signs of prolapse of the internal genitals, confirmed by clinical and ultrasound data, were found in 45% of patients in the main group, in the control group this pathology was not revealed. Birth injuries of newborns from mothers with uBD were diagnosed in 38% of cases versus 3.9% in the control group. This study showed that patients with generalized manifestations (involvement of three or more organs in the connective tissue defect) of uBD, even in the absence of severe forms of this pathology, are at high risk for the formation of obstetric and neonatal pathology [4].

CONCLUSIONS

Thus, pregnant women with signs of various forms of uBD belong to the high-risk groups for obstetric and perinatal pathologies and therefore need to be closely monitored during pregnancy, childbirth and the postpartum period. In addition, newborns who have a high probability of inheriting this disease must be examined. The high incidence of complications during pregnancy, childbirth and postpartum in patients with uBD determines the relevance of this problem in obstetrics and the thoroughness of the study of this category of women. However, ambiguous and sometimes contradictory data on the association and incidence of these complications with uBD require further research to establish a range of diagnostic and preventive measures.

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