American Journal of Medicine and Medical Sciences 2024, 14(5): 1182-1186
DOI: 10.5923/j.ajmms.20241405.08

The Significance of Connective Tissue Dysplasia in Structural and Functional Changes in the Respiratory System in Children

Akhmedova Nilufar Rasulovna, Atabaeva Ozoda Fakhriddinovna

Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan

Abstract The article presents an analysis of the literature, which reflects the influence of connective tissue dysplasia on structural and functional changes in the respiratory system in children, indicating the significant importance of connective tissue dysplasia in changing the clinical picture of respiratory diseases, including pneumonia, which greatly complicates their diagnosis, contributes to the formation of numerous complications.

Keywords Children, Connective tissue dysplasia, Respiratory diseases, Pneumonia

1. Introduction

Connective tissue dysplasia (CTD) remains an important problem in pediatrics due to its widespread prevalence, influence on the formation of chronic pathology, disability, and requires close attention [39,2,28,30].

The complexity of the organization of connective tissue, its ubiquitous presence in the organs and tissues of the body and the many functions it performs leads to the fact that the clinical manifestations of connective tissue defects are extremely diverse [26,28,31].

Connective tissue forms the supporting frame (skeleton) and the outer covering (skin); forms the internal environment of the body with blood and lymph; participates in the regulation of metabolic and trophic processes. The cellular elements of connective tissue are represented by fibroblasts and their varieties (osteoblasts, chondrocytes, odontoblasts, keratoblasts), macrophages (histiocytes) and mast cells (mast cells). The extracellular matrix is represented by 3 types of fibers: collagenous, reticular and elastic. CT performs 5 main functions: biomechanical (support-framework), trophic (metabolic), barrier (protective), plastic (reparative) and morphogenetic (structural-educational) [2,4,28,31].

The unique structure and functions of connective tissue creates conditions for the occurrence of a huge number of its anomalies and diseases caused by gene defects that have a certain type of inheritance, or due to the mutagenic effects of unfavorable environmental factors in the fetal period (unfavorable environmental conditions, unbalanced nutrition, stress, etc.) [28,2,30].

Currently, the term “connective tissue dysplasia” (CTD) is understood as an abnormality of tissue structure with a decrease in the content of certain types of collagen or a violation of their ratio, which leads to a decrease in the strength of the tissue of organs and systems. The consequence of this is a disorder of homeostasis at the tissue, organ and organism levels, which is accompanied by various morphofunctional disorders of the visceral and locomotor systems with a progressive course) [28,2,31].

The main causes of DST include changes in the rate of synthesis and assembly of collagen and elastin, synthesis of immature collagen, disruption of the structure of collagen and elastin fibers due to their insufficient cross-linking. This indicates that in DST, connective tissue defects in their manifestations are very diverse. The basis of these morphological disorders are hereditary or congenital mutations of genes directly encoding connective tissue structures, enzymes and their cofactors, as well as unfavorable environmental factors. In other words, DST is a multi-level process, because it can manifest itself at the gene level, at the level of imbalance of enzymatic and protein metabolism, as well as at the level of disruption of the homeostasis of individual macro- and microelements. In recent years, special attention has also been drawn to the pathogenetic significance of diselementosis, in particular hypomagnesemia [3,8,9,13].

Connective tissue, the share of which in the body makes up more than half of the body weight, performs numerous functions and responds to all physiological and pathological influences, and its damage leads to secondary disorders of internal organs and systems, the development of diseases [5,12,17,42].

In recent years, many researchers have obtained convincing data on the features of the course of a number of diseases associated with connective tissue dysplasia [6,12,13,15,16,17,18,35,30,36,37,39,40]. Connective tissue

Received: Apr. 20, 2024; Accepted: May 5, 2024; Published: May 7, 2024
Published online at http://journal.sapub.org/ajmms

dysplasia (CTD) is one of the most important and poorly understood problems. The authors interpret DST as a genetically determined disorder of the development of connective tissue, leading to a disorder of homeostasis at the tissue, organ and organism levels with a progressive course and determining the features of the associated pathology [10,38,43,20].

The literature widely presents works examining the characteristics of the heart, respiratory system, gastrointestinal tract, kidneys, blood, and nervous system in DST [13,1, 11,24].

The problem of studying the characteristics of the course of respiratory diseases against the background of CTD in children is very relevant, given the wide prevalence of connective tissue dysplasia, the variety of its clinical manifestations, and participation in the formation of chronic and recurrent processes of the respiratory tract [31,30,4].

DST leads to significant morphological and functional changes in the respiratory organs [5,12,17,42]. A congenital morphological defect of the cartilaginous and connective tissue framework of the trachea and bronchi ("softening") leads to increased mobility of the trachea and bronchi, the occurrence of bronchiectasis, and pneumosclerotic changes. An increase in the mobility of the trachea and bronchi during respiratory maneuvers was revealed - tracheobronchial dyskinesia with excessive invagination of the membranous wall (expiratory prolapse) with a high incidence of bronchospasm of the peripheral bronchi and the formation of broncho-obstructive syndrome (BOS) [12,34].

DST is associated with recurrent, chronic inflammation of the respiratory system, associated with impaired drainage function of the bronchi and changes in the viscosity of bronchial secretions. Anomalies in the structure of the bronchopulmonary system against the background of DST contribute to the deterioration of the elimination of pathogenic agents in conditions of altered immune reactivity [15,29].

In studies of the influence of DST on the structure and function of the bronchopulmonary system, a violation of the formation of the elastic framework of the lungs is noted: a change in the architecture of the lung tissue in the form of destruction of the interalveolar septa and underdevelopment of elastic and muscle fibers in the small bronchi and bronchioles, leading to reduced elasticity of the lung tissue with the formation of emphysematous bullae ; polycystic disease against the background of bronchial obstruction and the formation of spontaneous pneumothorax. A congenital defect in the cartilaginous and connective tissue framework of the trachea and bronchi leads to impaired mobility (dyskinesia), the occurrence of bronchiectasis, and pneumosclerosis. Tracheobronchial dyskinesia contributes to the development of bronchospasm [13,11,1,25].

The respiratory organ is under special conditions of constant physical activity, as a result of which the connective tissue proteins - collagen and elastin - are subject to completely different requirements than the proteins of the liver, kidneys and other organs. It is these proteins that determine the stability and pliability that are necessary to perform the main function - the function of gas exchange [8,27,32].

Morphological changes in the bronchopulmonary system in DST lead to changes in the function of the muscular-cartilaginous framework of the tracheobronchial tree and alveolar tissue, making them more elastic, which negatively affects the drainage function of the bronchi and the stromal stability of the alveoli [27,23].

Changes in the tracheobronchial tree are accompanied by dyskinesia of the airways (bloating on inhalation and collapse on exhalation, expiratory prolapse), the clinical manifestations of which (dry paroxysmal cough, chest pain in the projection of the tracheal bifurcation, attacks of difficulty breathing, simulating an attack of bronchial asthma (BA)) and changes in function external respiration (ER) depend on the local or diffuse nature of the lesion, the early appearance of complications, especially pulmonary emphysema. Primary diffuse pulmonary emphysema is associated with congenital weakness or atrophy of the elastic framework of the lungs. Since all connective elastic tissue suffers with emphysema, the elasticity of the bronchial wall decreases, therefore, with dynamic compression, it is not expiratory stenosis that occurs, but expiratory collapse, which results in impaired bronchial patency. The lumen of the intrapulmonary airways ceases to be stable, and the bronchi collapse even with a very slight increase in intrathoracic pressure. Chronic oxygen starvation can be clinically expressed in the development of severe asthenia, the formation of dystrophic changes in the heart muscle, deterioration of the functional state of the whole organism and aggravation of dysplastic-dependent changes in internal organs in conditions of increased sensitivity of abnormal collagen to changes in pH, which closes the pathological circle. With cystic underdevelopment of the bronchi, more pronounced disturbances in bronchial patency are detected than with acquired bronchiectasis, but the severity of diffusion disturbances is less than in the latter, which indicates the presence of compensation processes. DST leads to impaired elasticity of the lung tissue, which is accompanied by a tendency to develop emphysema, polycystic lung disease and spontaneous pneumothorax [8,23,27].

Structural and functional changes in the respiratory system in CTD, directly or indirectly associated with genetic defects of connective tissue structures, are extremely complex and are present to varying degrees in most patients with CTD [8,27]. In addition, bronchopulmonary dysplasia naturally changes the course of associated respiratory pathology. Children with DST often experience pneumonia with a more severe protracted course, there are features of the course of bronchial asthma, and they also more often develop obstructive bronchitis [15,41,25].

In children with DST, chronic bronchopulmonary pathology is very often detected. This syndrome in bronchopulmonary pathology occurs in 52-66.7% of cases, which significantly exceeds the population (9.8-34.3%) and confirms its role in the development of bronchial obstruction [4,2,30].

One of the most common associated pathologies in

DST associated with dysplastic-dependent changes in the bronchopulmonary system is community-acquired pneumonia. The morphological and functional features of the external respiration system discussed above in DST (impaired drainage function of the bronchi, impaired mucociliary clearance function, changes in the viscosity of bronchial secretions, the presence of deformation of the chest and spine, deterioration in the elimination of pathogenic agents in conditions of altered immune reactivity) create a favorable background for the development of the infectious process.

During inflammation, a cascade of pathophysiological reactions occurs, the most significant of which are disruption of the protease-inhibitor balance, as well as activation of lipid peroxidation with the formation of reactive oxygen species. Oxidative aggression is the direct cause of collagen destruction and leads to additional disturbances in the membrane architecture of structural elements. Macrophages and neutrophils destroyed during inflammation are the main source of proteases, the action of which leads to the destruction of interalveolar septa and the destruction of the elastic framework of the lungs, which naturally leads to the formation of centriacinar pulmonary emphysema - an irreversible and progressive component of bronchial obstruction. Anomalies in the structure of the bronchopulmonary system in DST contribute to the deterioration of the elimination of pathogenic agents in conditions of altered immune reactivity, as well as the long-term persistence of infectious agents, the formation of a recurrent course of pneumonia with predominant damage to interstitial tissue. In patients with DST, atypical pneumonia is more often formed, caused by intracellular pathogens (chlamydia, mycoplasma), with predominant damage to the interstitium of the lungs, with a recurrent course of which pneumofibrosis and pulmonary hypertension progresses [7,21,22,23,24]. Thus, bronchopulmonary dysplasia changes the course of associated respiratory pathology.

Such pronounced changes in the respiratory organs of a morphofunctional nature, as well as regulatory processes, could not but affect the clinical course of bronchopulmonary diseases, including pneumonia. Changes in the clinical course of pneumonia have recently been noted by many authors. Rapidly occurring pneumonia is less common. The number of patients with mild, asymptomatic forms of the disease, with a protracted course, with an outcome in chronic nonspecific diseases and pulmonary fibrosis has increased [33,41,25]. A.V. Papayan and his colleagues note that 48% of the examined children with pneumococcal pneumonia had a combination with respiratory chlamydia, which caused a longer course of pneumonia [29,15]. A feature of these pneumonias is the development of an inflammatory process in the interstitial, peribronchial, perivascular and perilobular connective tissue, in the lymphatic vessels of the lungs, with subsequent involvement of the alveoli, bronchioles in the inflammation process, with the accumulation of exudates in the alveoli. In pneumonia with predominant damage to the interstitium of the lungs, the intra-alveolar exudative component is less pronounced in comparison with typical ones, which causes frequent medical errors and is often regarded as an acute respiratory viral infection [41,39,34]. Considering the persistent course of infections caused by "atypical" pathogens (chlamydia, mycoplasma), pneumonia can acquire a recurrent course, being a source of pulmonary fibrosis, bronchiectasis, cystic changes in patients with DST, with possible subsequent transformation into interstitial lung diseases. A feature of the clinical course of atypical pneumonia (AP) is not only relapses, progressive deterioration with the formation of respiratory failure, but also the occurrence of spontaneous pneumothorax. The morphological basis of these changes is the formation of pneumofibrosis, cystic cavities against the background of DST [5,12,41]. Thus, the ontogenetic consolidation of hypoplastic deviation in the formation of both the respiratory organs and other organs and systems modifies the classic clinical symptoms of pneumonia. Conditions are created for gross medical errors, which contributes to the severe course of the disease and the emergence of complications.

Among the clinical features of bronchial asthma in this group of children, the following are noted: vegetative coloring of the attack, a high proportion of anomalies of the bronchial tree and minor anomalies in the development of the heart, the development of pulmonary hypertension, the predominantly proximal nature of bronchospasm, a small response to bronchospasmolytic drugs [4,2,39,25]. The involvement of several organs and systems simultaneously in the pathological process in children with CTD can explain the more severe, non-classical manifestation of clinical symptoms in diseases of the respiratory system, including prolonged pneumonia. The weakness of the connective tissue structures of the lung tissue predisposes to the development of various pathologies of the respiratory system [8,21,23,26].

2. Conclusions

Thus, an analysis of the literature reflecting this problem indicates the significant importance of connective tissue dysplasia in changing the clinical picture of respiratory diseases, including pneumonia, which significantly complicates their diagnosis and contributes to the formation of numerous complications. Therefore, studying the role of DST in changing the clinical course of prolonged pneumonia is relevant.

REFERENCES

[1] Abbakumova L.N., Arsentiev V.G., Gnusaev S.F. Hereditary and multifactorial connective tissue disorders in children. Diagnostic algorithms, management tactics. Project of Russian recommendations // Pediatrics. – 2014. – T. 93, No. 5. – 38 p.

[2] Arsentiev V. G., V. S. Baranov, N. P. Shabalov Hereditary diseases of connective tissue as a constitutional cause of multiple organ disorders in children / St. Petersburg Monograph 2015 P.11.

[3] Arsentiev V.G., Arzumanova T.I., Aseev M.V., Baranov V.S., Kalyadin S.B., Nikiforova I.D. and others. Multiple organ disorders in connective tissue dysplasia in children and adolescents // Pediatrics. 2009. T.87, No. 1. P. 135-138.

[4] Babtseva A.F., Shanova O.V., Boychenko T.E., Arutyunyan K.A., Romantsova E.B. Textbook Connective tissue dysplasia in children and adolescents // Blagoveshchensk 2010.

[5] Vlasov P., Karmazanovsky G. Cysts and cyst-like formations in the lungs // News of medicine and pharmacy. – 2005. – No. 3 (163). – pp. 23–24.

[6] Gavalov S.M. Features of clinical manifestations and course of various forms of bronchopulmonary pathology in children with minor forms of connective tissue dysplasia / S.M. Gavalov, V.V. Zelenskaya // Pediatrics. – 1999. – No. 1. – P. 49-52.

[7] Demin V.F., Klyuchnikov S.O., Klyuchnikova M.A. The importance of connective tissue dysplasia in the pathology of childhood // Issues of modern pediatrics. - 2005. - T. 4, No. 1. - P. 50-56.

[8] Evtushenko S.K., Lisovsky E.V., Evtushenko O.S. Connective tissue dysplasia in neurology and pediatrics: a guide for doctors. Donetsk: Publishing House "Zaslavsky", 2009. 361 p.

[9] Zemtsovsky E.V. Undifferentiated connective tissue dysplasia. No right to diagnosis! // Medical statements. 2010. No. 3(53). pp. 76-80.

[10] Zemtsovsky, E.V. Dysplastic phenotypes. Dysplastic heart. – St. Petersburg: Olga, 2007. – 80 p.

[11] Zemtsovsky E. V. Hereditary disorders of the structure and function of connective tissue: Russian national recommendations / ed. - Moscow, 2009. - 66 p.

[12] Kadurina T. I. Hereditary collagenopathies. – St. Petersburg, 2000. – 271 p.

[13] Kadurina, T.I. Connective tissue dysplasia: a guide for doctors / T.I. Kadurina, V.N. Gorbunova. – St. Petersburg: Elbi St. Petersburg, – 2009. – 714 p.

[14] Kondusova, Yu.V. Features of the course and rehabilitation of bronchial asthma associated with undifferentiated connective tissue dysplasia in children / Yu.V. Kondusova, A.V. Pochivalov // Pediatric aspects of connective tissue dysplasia. Achievements and prospects: Ros. Sat. scientific tr. – M.; Tver; St. Petersburg: PR100, 2011. – Issue. 2. – pp. 271-275.

[15] Logvinova O. P., Senatorova G. S., Buzhinska N. R. The role of the pathology of the resulting tissue in the formation of long-term bronchitis in children and children // Proceedings of the scientific-practical conference. – Kharkov, 2004. – pp. 87–90.

[16] Lyalukova, E.A. Anomalies of the pancreaticoduodenal zone in patients with connective tissue dysplasia: clinical manifestations, management tactics / E.A. Lyalukova // Siberian Medical Journal. – 2011. – T. 26, No. 3. – P. 74-76.

[17] Martynov A. I., Stepura O. B., Ostroumova O. D., Pak L. S. PMK. Part 1. Phenotypic features and clinical manifestations // Cardiology. – 1998. – No. 1. – P. 72–78.

[18] Marushko, Yu.V. Features of the course of respiratory diseases in children with signs of connective tissue dysplasia / Yu.V. Marushko, E.D. Moskovenko // Pediatric aspects of connective tissue dysplasia. Achievements and prospects: Ros. Sat. scientific tr. – M.; Tver; St. Petersburg: PR100, 2011. – Issue. 2. – pp. 275-281.

[19] Nesterenko Z. V. Bronchial asthma in children with manifestations of connective tissue dysplasia: features of the clinical course, complications. Medical Bulletin of the Northern Caucasus 2016. T. 11. No. 2. Issue. 2. P.280-282.

[20] Nesterenko Z.V. Connective tissue dysplasia and the current course of pneumonia in children. Kuban Scientific Medical Bulletin No. 6 (111) 2009. P.62-64.

[21] Nesterenko Z.V. New aspects in the treatment of recurrent atypical pneumonia in children with congenital connective tissue dysplasia // Perinatology and Pediatrics. - 2007. - No. 4(32). — P. 85-87.

[22] Nesterenko Z.V. Features of the clinical course of respiratory diseases in children with congenital connective tissue dysplasia // Ukrainian Medical Almanac. - 2005. - No. 5. - P. 111-117.

[23] Nesterenko Z.V. The phenomenon of connective tissue dysplasia // Ukrainian Medical Almanac. - 2008. - No. 4. - P. 105-109.

[24] Nesterenko Z.V., Soldatenkova E.V., Natalchenko G.I. Features of atypical pneumonia in children with mesenchymal dysplasia // Mat. scientific-practical conf. "The pathology of healthy tissue is the basis for the formation of chronic illnesses in children and children." - Kharkiv, 2004. - P. 100-102.

[25] Nesterenko, Z. V. Features of respiratory diseases in children with connective tissue dysplasia / Z. V. Nesterenko, A. A. Gritsai. – Kharkov: "Shchedra sadiba plus", 2014. – 205 p.

[26] Nechaeva G., Viktorova I., Druk I. Connective tissue dysplasia: prevalence, phenotypic signs, association with other diseases // Doctor. - 2006. - No. 1. - P. 19-23.

[27] Nechaeva G.I., Viktorova I.V., Druk I.V., Vershinina M.V. Connective tissue dysplasia: pulmonological aspects // Pulmonology. - 2004. - No. 2. - P. 116-120.

[28] Osipenko I.P. Biochemical markers of undifferentiated connective tissue dysplasia in patients with idiopathic mitral valve prolapse // Russian Medical and Biological Bulletin named after Academician I.P. Pavlova. 2013. No. 1. pp. 38-44.

[29] Papayan A.V., Nikitina M.A., Vishnyakov L.A. Features of the clinical course of pneumonia in children against the background of chlamydial infection // Ros. Bulletin of Perinatology and Pediatrics. – 2004. – No. 4. T. 49. – P. 42–51.

[30] Paramonova N.S. Features of the course of chronic diseases of the stomach and duodenum in children with connective tissue dysplasia / N.S. Paramonova, A.A. Krchevsky // Pediatric aspects of connective tissue dysplasia. Achievements and prospects: Ros. Sat. scientific tr. – M.; Tver; St. Petersburg: PR100, 2011. – Issue. 2. – pp. 204-208.

[31] Pochivalov A.V., Ivannikova A.S., Bugrimov D.Yu., Tsvetikova L.N. The influence of connective tissue dysplasia on the course of respiratory pathology in children. Scientific bulletins, medicine series. Pharmacy. 2013. No. 25 (168). Issue 24. P. 45-49.

[32] Ryvkin A.I., Orlova S.N., Pobedinskaya N.S. Connective tissue dysplasia syndrome in children with stenosing laryngotracheitis // Pediatrics. - 2006. - No. 3. - P. 10-14.

[33] Samsygina G. A. Respiratory tract infections in young children.

– M., 2006. – 279 p.

[34] Tatochenko V.K. Practical pulmonology of childhood / Ed. V. K. Tatochenko. – M., 2000. – P. 167–183.

[35] Timofeeva E.P., Ryabichenko T.I., Kartseva T.V., Skosyreva G.A. Features of the course of chronic pyelonephritis in children and adolescents against the background of connective tissue dysplasia // Siberian Medical Journal. – 2011. – T. 26, No. 3. – P. 53-56.

[36] Trutneva, L.A. Features of gastroduodenal diseases in children with undifferentiated connective tissue dysplasia / L.A. Trutneva, V.V. Suitcases // Pediatrics. – 2010. – T. 89, No. 2. – P. 12-17.

[37] Uzunova A.N. Features of renal hemodynamics in children with chronic secondary pyelonephritis that developed against the background of connective tissue dysplasia / A.N. Uzunova, A.Yu. Kinzersky, L.V. Glukhova // Pediatrics. – 2006. – No. 5. – P. 10-12.

[38] Utz I.A. Undifferentiated connective tissue dysplasia in children / I.A. Utz, E.N. Gorodkova // Pediatrics. – 2008. – T. 87, No. 2. – P. 117-119.

[39] Suitcases V.V. Features of the course of diseases in children with connective tissue dysplasia / V.V. Chemodanov, E.E. Krasnova. – Ivanovo: State Educational Institution of Higher Professional Education IvSMA Roszdrav, 2009. – 140 p.

[40] Suitcases, V.V. Connective tissue dysplasia: more questions than answers / V.V. Chemodanov, E.E. Krasnova // Pediatric aspects of connective tissue dysplasia. Achievements and prospects: Ros. Sat. scientific tr. – M.; Tver; St. Petersburg: PRE100, 2010. – P. 93-100

[41] Chuchalin A. G., Sinopalnikov A. I., Strachunsky L. S. Pneumonia. – M.: honey. information agency, 2006. – 462 p.

[42] Shakhnazarova M. D., Rozinova N. N. Damage to the bronchopulmonary system in monogenic connective tissue diseases // Ros. Bulletin of Perinatology and Pediatrics. – 2004. – No. 4. T. 49. – P. 11–13.

[43] Yakovlev V.M. Connective tissue dysplasia of the mitral valve / V.M. Yakovlev, R.S. Karpov, E.V. Shvetsova. – Tomsk: Siberian Publishing House, 2003. – 144 p.