STRUCTURAL CHANGES IN REGIONAL LYMPH NODES IN EXPERIMENTAL PULMONARY FIBROSIS

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ABSTRACT: Pulmonary fibrosis is a pathological process in the lungs characterized by refractoriness to therapy and high mortality rates, it represents a heterogeneous group of disorders with progressive and irreversible destruction of lung architectonics due to scarring, which ultimately leads to organ dysfunction, gas exchange disorders and death due to respiratory failure. [D.V. Bestaev, 2014]. But changes in the lymph nodes during the fibrous process of the lung tissue are poorly understood. The article presents a review of the literature on structural changes in regional lymph nodes that occur in experimental pulmonary fibrosis.

KEYWORDS: pulmonary fibrosis, regional lymph nodes, laboratory experiment.

INTRODUCTION

The pandemic of a new coronavirus disease in 2019 (COVID-19), caused by the SARS-CoV-2 coronavirus, has given rise to serious concern among the world community due to its rapid spread, high mortality rate and lack of specific and effective treatment (in the first 4 months after the outbreak was reported, about 3 million people and 200,000 people were infected with SARS-CoV2 infection died) [WHO Bull, 2020].

Like the previous strains (SARS-CoV and MERS-CoV) of the coronavirus family, SARS-CoV2 primarily affects the respiratory system, causing infection of the lower respiratory tract and serious complications in the lungs, including acute respiratory distress syndrome (ARDS), which is the main cause of death of coronavirus patients [Aitbayev K. A., 2021]. As for the patients who survived ARDS, a significant part of them will have long-term lung dysfunction due to the development of fibrosis. It is
important to note that pulmonary fibrosis is a generally recognized consequence of ARDS and, as has been shown in several studies, the so-called "protective ventilation" of the lungs reduced radiological abnormalities after ARDS [Burnham E. L., et.all., 2014].

The pathological correlate of ARDS is diffuse alveolar lesion (DAP), which is characterized by an initial (acute inflammatory) exudative phase with edema, hyaline membranes and acute interstitial inflammation, followed by an organization phase with loose organizing fibrosis, mainly inside the alveolar septa and hyperplasia of type II pneumocytes [Cardinal-Fernández P., et.all., 2017]. A powerful third and final stage of ARDS may be the fibrous phase. Thille and co-authors described a cohort of 159 autopsies of patients with ARDS, showing that these pathological findings can either resolve to normal lung parenchyma or progress to fibrosis [Thille A. W., et.all., 2013]. It is important to note that there is evidence that progressive pulmonary fibrosis may be the cause of death in many patients with ARDS, while a significant proportion of survivors will have long-term lung dysfunction and radiological abnormalities indicating pulmonary fibrosis. [Burnham E. L., 2013].

Recent studies show that mesenchymal stromal cells are capable of destroying the pathological extracellular matrix by secreting a variety of matrix metalloproteinases, as well as inhibiting the progression of fibrosis due to paracrine factors secreted by cells and extracellular vesicles carrying various non-coding microRNAs. However, the mechanisms of this effect are still poorly understood. [A.Efimenko, 2020].

I.V.Davydovsky pointed out that with pneumosclerosis, scar fields in the lung often undergo smooth muscle transformations ("muscular cirrhosis") due to constant respiratory excursions of the organ.

A number of scientists under "pneumosclerosis" describe chronic scarring and degenerative changes developing both in the alveoli and in the interstitial tissue between the lobules, along the bronchi, in the walls of the bronchi themselves [S.O.Neville, 1963]. At the same time, the blood vessels of the lungs, nerve trunks and lymphatic vessels are involved in the process. Moreover, pneumosclerosis is not an independent nosological form.

The process of fibrogenesis in response to damage is realized through complex cellular interactions, in which certain molecular pathways are important [Maher T.M., 2012]. There are 4 main phases of fibrogenesis: the 1st phase is the initiation of a response caused by primary organ damage, the 2nd phase is characterized by the activation of effector cells, in the 3rd phase the extracellular matrix is produced, in the 4th - dynamic deposition (and insufficient resorption) of the extracellular matrix. The second and third phases, together with the fourth, contribute to the progression of fibrosis, damage to organ tissue [N.A. Shostak, A.A. Klimenko, A.A. Kondrashov, 2017].
There are models of the development of pulmonary fibrosis in the experiment. The problem of creating an effective experimental model of pneumosclerosis is due to the polyetiology and heterogeneity of this disease. Various factors and pathogenetic pathways contribute to the development of the disease, influencing the formation of chronic inflammation, damage to the small bronchi, destruction of the pulmonary parenchyma and vascular system of the small circulatory system [Zolotnitskaya V.P., 2017]. Nitrogen oxides play an important role in the development of environmentally caused lung diseases (chronic obstructive pulmonary disease, bronchial asthma, pulmonary interstitial fibrosis), initiating damage and death of bronchoalveolar epithelial cells. One of the most aggressive anthropogenic pollutants is nitrogen dioxide (NO2), the content of which in the atmosphere of megacities can be ten times higher than hygienic standards. The main source of NO2 is emissions from motor vehicles, power plants and boiler houses (during the combustion of organic fuel), chemical and metallurgical enterprises. The concentration of this pollutant is considered a marker of air pollution by automobile exhaust. American Environmental Protection Agency [Environmental Protection Agency (EPA)] included NO2 (along with ozone, carbon monoxide, sulfur dioxide, lead and suspended particles) in the top six air pollutants ("criteria air pollutants") [EPA, 2013]. In 2010 EPA, in order to protect public health, has established a standard for NO2 content (average content for 1 hour) of 0.1 particles per 1 million (0.188 mg/m3). However, so far no US region meets this standard. [O.N. Titova, et al., 2014].

There is a direct connection of the lymphatic system with the lungs. The lymphatic channel transports tissue fluid from the lesion into the blood and can be considered as an organ that ensures the constancy of the volume of plasma and interstitial fluid [Kozlov V.I., 2005; Sapin M.R. et al., 2007; Banin V.V., 2014]. The lymphatic system is arranged as a chain of intervalvular segments with different wall structures, organizes a special outflow path from the organs (collateral drainage to the veins) of tissue fluid in the form of lymph, and in its composition – antigens. The lymphoid system looks like a special prefix of the cardiovascular system: lymphoid couplings of varying complexity of structure surround tissue channels and vessels as their nozzles-biofilters that regulate the cellular and protein composition of the internal environment of the body. The lymphoid system is based on blood vessels closed in a circle, through which lymphocytes (re)circulate. The lymphatic bed drains lymphoid formations, brings lymph to some of them for purification. The lymphoid and lymphatic systems are combined on the periphery into an immunoprotective complex: the lymphatic bed and lymphoid tissue around the blood microvessels cooperate to ensure genotypic homeostasis of the body, make up the lymphoid-lymphatic apparatus as part of the cardiovascular system. The lymphatic system participates in the organization of immunity in humans.
and animals, since the lymphatic channel carries out the influx of antigens into the lymph nodes and simpler lymphoid formations (lymphoid nodules and plaques) with afferent lymphatic pathways.

Lymph nodes are organs of the lymphatic system that perform the function of a biological filter and provide a number of vital functions: they delay foreign particles, toxins that have entered the blood, fight against foreign bacteria and viruses. The average size of healthy lymph nodes is from 5 millimeters to 1 centimeter. According to the literature, it is known that lymph nodes react dynamically and labilely to the effects of endogenous and exogenous intoxication of the body by changing their structural and functional features [Borodin Yu.I., 1992; Rudaev A.I., 1997; Huseynov T.S. et al., 2015]. Relatively few works have been devoted to the study of all components of the lymphatic system of humans and experimental animals, with pathology resulting from intoxication with nitrogen dioxide. In this regard, all of the above opens up prospects for an in-depth morphological study of the restructuring of regional lymph nodes in fibrotic pathology of the lungs, and in organs remote from the lesion in the dynamics of the early inflammatory process leading to pneumosclerosis of the lungs, as well as the search for ways to correct them.

Currently, it is becoming obvious that the traditional therapy of inflammatory lung diseases, based primarily on antibiotics, is becoming less effective. The success of the treatment of lung diseases is largely due to the search for new therapies, including those based on the stimulation of regenerative reactions. The fundamental experimental base on regenerative processes in the lungs is presented in the studies of L.K. Romanova (1984, 1987). Inflammatory lung diseases are accompanied by stereotypical structural transformations of the organ and its regional lymphatic structures. Their complex includes dystrophic, necrobiotic, sclerotic, atrophic compensatory and adaptive processes. [Polosukhin V.V., 1997].

Conclusions

Each inflammatory process in the lungs is reflected in the lymph nodes, sometimes only in the regional, sometimes in the extra-thoracic and distant ones. Their reaction in response to lung infection in the form of an increase in children is much stronger and more frequent than in adults, and any inflammatory process in the lungs can be followed by an increase in regional nodes.

Structural transformations in regional lymph nodes during inflammation in the region are determined by the level of development and activity of the inflammatory response, includes a wide range of alterations, a decrease in immune reproducing function, but with the preservation of the barrier. A decrease in the activity of the inflammatory reaction in the region, in accordance with this, a decrease in the toxic influence of the region is accompanied by a rapid restoration of the structural organization of the lymph nodes.
In general, the study of available literature data revealed a lack of information on the effect of pulmonary fibrosis on the structural and morphological state of the tissue of regional lymph nodes.

The little-studied nature of this problem makes it possible to further study it and search for new methods of treatment, as well as the development of new medicines to correct these changes.

References


