Horizon | Journal of Humanity and Artificial Intelligence

MODERN VIEW ON THE PATHOGENETIC MECHANISMS OF BRONCHIAL ASTHMA IN CHILDREN

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Abstract

This review article is devoted to modern aspects of studying the pathogenesis of one of the most significant allergic diseases, bronchial asthma (BA). Despite the successes achieved in evidence-based medicine and clinical pharmacology, the treatment of AD remains a difficult task today, due to the continuing trend towards an increase in severe cases, insufficient control of the disease in most patients, the use of systemic glucocorticosteroids in some patients, and poor quality of life. To solve the problem of AD, it is necessary to delve deeper into the main pathogenetic links of the allergic process. In this article, the authors have studied the modern principles of the pathogenesis of AD, systematized and analyzed foreign studies.

Keywords: Bronchial asthma, immunity, children, pathogenesis.

Introduction. The incidence of AD is increasing worldwide. It is among the top ten non-communicable chronic diseases that are the main cause of death in middle and old age, reducing the average life expectancy of men by 6.6 years, women by 13.5 years. Today there are about 300 million patients with AD in the world. (Report of the Second World Assembly on Aging Madrid; 2011.). Despite the large amount of information in the available literature, there is no information whether the age of patients in which the disease developed can affect its manifestations and course [9].

BA leads to permanent disability, to a decrease in the quality of life, as well as mortality. According to statistics, there are about 130 million patients. The fear of an attack, which can manifest itself in AD, does not allow you to do simple work, and the symptoms of the course lead to patient care for several days [12].

Bronchial asthma (BA, J46) is a heterogeneous disease, mainly characterized by chronic inflammation of the respiratory tract. It is diagnosed on the basis of respiratory symptoms in the form of wheezing, difficulty breathing, tension and chest swelling, cough. Symptoms may vary in time and severity in parallel with the variation of difficulty exhaling [1]. Thus, AD is a chronic inflammation of the respiratory tract, in which many cells are involved, especially mastocytes, eosinophils and T-lymphocytes. In individuals genetically predisposed to AD [2], this inflammation leads to repeated episodes of wheezing, coughing, shortness of breath, chest swelling. This condition is widespread, but the resulting obstruction of the respiratory tract is resolved either independently or under the influence of treatment. Inflammation is also the cause of bronchial hyperreactivity in response to a variety of stimuli [3]. The main thing in the definition of BA is an indication of inflammation and spasm of the respiratory tract, which justifies the choice of drugs.

The growth of allergic diseases in children makes in-depth studies of the pathogenesis of this pathology and the search for effective therapies relevant. BA in children is one of the most common chronic diseases. According to the results of meta-analysis, the prevalence of AD in children is 5.3% on average [4]. The prevalence of allergic rhinitis (hereinafter referred to as AR) ranges from 10 to 24% [5]. The number of combined forms of allergic pathology is growing [6].

Over the past decades, an increase in the prevalence of allergic diseases has been recorded worldwide, due to both the impact of environmentally unfavorable environmental factors, changes in the socio-economic situation, and improved diagnosis of such diseases. Among this group of pathology, BA, one of the most frequent chronic diseases of the bronchopulmonary system, is of the greatest interest from a scientific and practical point of view.

BA is common in all age groups, characterized by high rates of spread, especially in countries with low socio-economic standard of living of the population, and is a global health problem. In addition to significant costs for treatment and prevention, AD often causes the death of patients, including younger children [7]. Diagnosis of AD at an early age is difficult due to the peculiarities of its formation and course in patients of this cohort [8]. It is no coincidence that making this diagnosis in children 5 years and younger, according to the GINA (Global Initiative for Asthma – Global Strategy for Treatment and Prevention) 2020 program document, is associated with objective difficulties and requires careful differential diagnosis [7]. Asthma in this age group is characterized by a complex of etiological and pathogenetic features, which cannot but determine, in turn, approaches to its diagnosis and therapy [9].

Viral infections such as respiratory syncytial virus (RSV) and human rhinovirus (HRV) have been implicated in exacerbating asthma in children due to their ability to cause severe inflammation of the respiratory tract and wheezing. Infections with atypical bacteria also seem to play a role in the induction and exacerbation of asthma. Recent studies confirm the existence of an infectious etiology of asthma mediated by Chlamydia pneumoniae (CP) and possibly other viral, bacterial and fungal microbes. It is also likely that early infections with microbes such as CP can lead to changes in the lung microbiome that significantly affect asthma risk and treatment outcomes. These infectious microbes can aggravate the symptoms of established chronic asthma and may even contribute to the initial development of the clinical onset of the disease. It is now increasingly recognized that the patterns of airway inflammation differ depending on the trigger responsible for the initiation and exacerbation of asthma. Thus, a deeper understanding of asthma subtypes is currently being studied more actively, not only to decipher pathophysiological mechanisms, but also to choose treatment and prognosis [11].

Numerous scientific studies devoted to the study of the pathogenesis of AD have significantly expanded the understanding of this pathology. Developments in the field of immunology research are of interest. Violations on the part of the programmed "physiological" cell death of immunocompetent cells lead to the development of the disease due to an inadequate immune response to any endo- and/or exogenous exposure [15].

Of the environmental factors that can lead to the development of bronchoobstructive syndrome (BOS), special importance is attached to passive smoking. Under the influence of tobacco smoke, hypertrophy of the bronchial mucosal glands occurs, mucociliary clearance is disrupted, the progress of mucus slows down. Passive smoking contributes to the destruction of the bronchial epithelium. With prolonged exposure, tobacco smoke has an effect on the immune system: it inhibits neutrophil chemotaxis, reduces the activity of T-lymphocytes, inhibits the synthesis of antibodies of the main classes of immunoglobulins, stimulates the synthesis of immunoglobulin E, increases the activity of the vagus nerve.

The following mechanisms are responsible for the occurrence of bronchial obstruction:

- ✓ dystonia of the bronchial wall,
- ✓ hypertrophy of muscle tissue,
- ✓ hypercrinia and dyscrinia,
- ✓ bronchospasm,
- ✓ violation of mucociliary clearance,
- ✓ edema,
- ✓ inflammatory infiltration,

- ✓ hyperplasia and metaplasia of the mucous membrane,
- ✓ compression, obturation and deformation of the bronchi,
- ✓ defects of local and systemic immunity, defects of the macrophage system.

Cytokines play a role in the regulation of immune processes developing in the human body. Cytokine synthesis suppresses the development of an immune response and inflammation. The problems of functioning of the immune system, understanding of the molecular mechanisms of cytokine action on target cells, their symbiotic relationships between themselves and the respiratory, nervous system are important not only to identify the physiological foundations of the immune system, but also to further the level of quality of life [14].

Bronchoalveolar lavage (BALJ) allows you to assess the state of the local immunity link of the respiratory tract, to characterize the cellular link of immunity, to study the level of cytokines. Violation of the production and reception of anti-inflammatory cytokines leads to deep defects in anti-infective protection, up to the development of an immunodeficiency state and aggravates the direct damaging effect of microorganisms and their toxins on lung tissue. The leading role in the formation of a prolonged course of inflammatory diseases of the respiratory tract in children and adolescents belongs to immunological mechanisms, which involve a large range of cytokines responsible for activation, proliferation and chemotaxis of various cells. The greatest role in chronic obstructive bronchitis (COPD) is played by interleukin-8 (IL-8). It is able to destroy the structure of the lungs and maintain neutrophilic inflammation. It is present in high concentrations in induced sputum and lavage in patients with COPD [13].

Interleukin-1ß (IL-1ß) is a member of the IL-1 cytokine family. This cytokine is an important mediator of the inflammatory response, and is also involved in various cellular activities, including cell proliferation, differentiation and apoptosis. The synthesis of IL-1ß begins in response to the introduction of microorganisms or tissue damage and triggers a complex of protective reactions that make up the first line of defense of the body [12].

The course and outcome of the inflammatory process are controlled by anti-inflammatory cytokines. The main local protective factors responsible for limiting bacterial proliferation are secretory immunoglobulin-A (sIgA). sIgA is present throughout the respiratory tract and refers to markers of local immunity. The main functions of sIgA are to protect the mucous membrane by neutralizing toxins and viruses, and block bactrial adhesion to epithelial cells. Moreover, sIgA has a protective effect exclusively in the composition of mucus [10].

Since the mucous membrane of the nasal cavity is rich in vessels, and the lower respiratory tract has a well-developed peribronchial smooth muscle, acute obstruction of the nasal cavity is mainly the result of vascular dilation, while bronchial obstruction is mainly due to spasm of the smooth muscles of the bronchi. The systemic pathway of the relationship of the upper and lower respiratory tract includes the bloodstream and bone marrow [16].

Numerous studies of recent years serve as proof of the systemic nature of allergic inflammation. Local allergen-specific provocation of both the nasal mucosa and the bronchi leads to the generalization of allergic inflammation. 24 hours after intranasal provocation with a causally significant pollen allergen, statistically significant involvement of eosinophils was noted in patients with AR without BA not only in the nasal mucosa, but also in the bronchial mucosa. The number of eosinophils in the nasal mucosa correlates with the local expression of ICAM-1, E-selectin and VCAM-1. Segmental bronchial provocation in patients with AR without BA leads to an increase in the number of eosinophils and increased expression of IL5 in the nasal epithelium 24 hours after provocation [14,15].

Conclusion

These facts substantiate the concept of "unified airways", which demonstrates the close relationship between allergic rhinitis and asthma and proves that the inflammatory response can be maintained and enhanced by interrelated mechanisms. Even in the absence of clinical manifestations of the acute phase

of an allergic reaction (rhinorrhea, itching, sneezing), an intranasal provocative test in children and adults with AR increases the signs of allergic inflammation of the bronchial mucosa. These studies indicate that the current allergic inflammation in the nasal cavity, the ongoing antigenic stimulation of the respiratory tract lead to the spread and intensification of allergic inflammation and may contribute to the manifestation of AD. Therefore, patients with allergic rhinitis should be examined for the presence of AD. Currently, the issue of identifying the most significant risk factors affecting the realization of AD in children remains insufficiently studied, which must be taken into account when developing methods for forecasting and conducting individual preventive measures.

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