

DISCLOSURE OF ISSUES OF PATHOGENESIS OF ALLERGIC PATHOLOGY OF CHILDHOOD

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Abstract

The presence of atopic genesis of allergic pathology in children is confirmed by the detection of overproduction of total IgE, specific IgE antibodies, and positive skin tests with allergens. The group of patients classified as atopic, is based on identifying a family predisposition to allergic reactions and diseases and obtaining evidence of the leading role of the IgE-mediated mechanism in their development.

Keywords: allergy, allergic rhinitis (AR), allergic dermatitis (AD), prevalence, urticaria, allergic reactions, bronchial asthma, IgE.

Introduction

RELEVANCE OF THE TOPIC

Allergic diseases are the most common and common pathology in pediatrics. The incidence of the disease ranges from 14% to 34% of the child population. Allergic diseases detected in children are in most cases of atopic origin. The presence of atopy is confirmed by the detection of overproduction of total IgE, specific IgE antibodies, and positive skin tests with allergens. At the initial stage of development, atopy can manifest itself only at the level of immune changes (detection of overproduction of general and specific IgE) and the connection of atopy with a specific genetic marker - a candidate gene located on chromosome 11q13. The occurrence of clinical manifestations of atopy is a consequence of the activation of cells involved in the IgE-mediated allergic process, such as mast cells, basophils, and eosinophils.

PURPOSE OF THE RESEARCH

Study of the pathogenesis of allergic pathology in childhood.

MATERIALS AND METHODS OF RESEARCH

The study was carried out in the Andijan Regional Children's Clinical Hospital in the pulmonology department. 100 children with bronchial asthma, aged from 1 to 5 years, were examined, of which 42 (42%) children were aged from 1 to 2 years, 58 (58%) children were from 3 to 5 years. Among the observed children, there were 16 (16%) with a mild

intermittent course of bronchial asthma, 42 (25%) with a mild persistent course, 25 (25%) with a moderate course and 17 (17%) children with a severe course of bronchial asthma. In addition, children with atopic dermatitis were examined - 84 people, whose age ranged from 2 to 15 years, with allergic rhinitis - 67 people, whose age ranged from 8 to 14 years.

RESULTS OBTAINED

Atopy determines the development of many allergic diseases in children, primarily atopic dermatitis (AD), bronchial asthma (BA), and allergic rhinitis (AR). The classification of this group of diseases as atopic, is based on identifying a family predisposition to allergic reactions and diseases and obtaining evidence of the leading role of the IgE-mediated mechanism in their development.

AD is an early manifestation of atopy in children. This disease is considered by allergists and many dermatologists as a clinical marker of the presence of atopy in a patient. AD occurred in 72 (86%) children if both parents had AD, in 38 (45%) - in cases where one of the parents had AD and the other had a respiratory allergy, and in 42 (50%) - if one of the parents had AD.

Blood pressure had a delineated clinical picture of the disease, undergoing certain changes with the age of the patients. The infancy period (from the onset of the disease to 2 years) was characterized by acute and subacute inflammatory changes in the skin, with a tendency to exudate. The childhood period (from 2 to 10 years) was characterized by the absence of exudative manifestations and the appearance of erythemo-infiltrative, squamous and lichenoid foci with localization of the inflammatory process in the folds of the skin. In adolescence, lesions in the skin folds are replaced by diffuse lesions of the skin of the face, neck, upper body and extremities with a predominance of lichenized and infiltrated lesions, lichenoid papules and excoriations. In addition to the occurrence of these symptoms, AD was manifested by eczema of the hands, feet, nipples, cheilitis, cracks and weeping behind the ears.

The most important signs for diagnosing AD were the following: 1) itchy nature of the rash (the absence of itching is not typical for AD); 2) detection of lichenification of the skin in the elbow and knee bends; 3) onset of the disease in early childhood; 4) chronic relapsing course of the disease; 5) identification of heredity burden with allergic reactions and diseases; 6) detection of increased levels of total and specific IgE in the blood serum. Auxiliary (additional) signs of AD were the following: the presence of food allergies, dryness, darkening of the eyelids, Denis-Morgan folds of the lower eyelid, pallor or congestive erythema of the facial skin, white dermographism, blood eosinophilia, hyperlinearity of the palms, keratosis pilaris, complications (conjunctivitis, keratoconus, cataract).

According to an allergological examination, an increase in the level of total IgE in the blood serum is found in 92% of children with AD, and specific IgE antibodies to various allergens were detected in 84% of cases, while in young children suffering from AD, the leading role in the development of the disease was played by food allergies, in subsequent age periods

the value of sensitization to house dust allergens, *Dermatophagoides pteronyssimus*, *Dermatophagoides farinae*, epidermal, pollen allergens, mold spore allergens increases. Some pediatricians also include other skin lesions as manifestations of AD, such as seborrheic dermatitis, microbial eczema, strophulus, diaper dermatitis, ichthyosis, fungal skin lesions, psoriasis, Wiskott-Aldrich syndrome. However, these diseases have nothing in common with atopy. Based on an assessment of the manifestations of the disease, the results of a clinical and, if necessary, allergological examination, the true nature of the disease was established.

Asthma is one of the most common diseases in childhood. The development of asthma in children is in most cases associated with atopy. According to an allergological examination, the atopic form of asthma was diagnosed in more than 90% of children with asthma. In the remaining children, the role of infectious allergies in the development of asthma was previously recognized. This was confirmed by the identification of a connection between exacerbation of asthma and the addition of infectious diseases, exacerbation of foci of chronic infection, positive skin tests with bacterial allergens, and specific IgE antibodies to bacterial antigens. Thus, in 46 (46%) children with asthma with identified sensitization to staphylococcus, increased production of specific IgE antibodies to the allergens of this microorganism was recorded, which gives grounds to consider the possible involvement of infection in the pathogenesis of asthma through an IgE-mediated mechanism. It is possible to form specific IgE to various respiratory viruses.

The participation of atopy in the development of asthma in children is evidenced by the discovery in more than 87 (87%) patients of hereditary burden of allergic reactions and diseases, including asthma. A high-risk factor for the occurrence of AD is the development in children suffering from AD of sensitization to the allergens *Dermatophagoides pteronyssimus*, *Dermatophagoides farinae* and pollen allergens. The importance of atopy in the pathogenesis of asthma in children is evidenced by the discovery in 95 (95%) of them of increased levels of total IgE and specific IgE antibodies to various groups of allergens. In 72 (72%) patients with asthma, bronchial hyperreactivity is detected, which is largely genetically determined. Increased IgE production and bronchial hyperreactivity are inherited together and are controlled by genes located on chromosome 5q. Genetic susceptibility to AD can also be realized at the level of β -adrenergic receptor genes, as well as genes that control the synthesis of mediators, proinflammatory cytokines, and germ factors.

As a disease, asthma is characterized by a polymorphism of clinical manifestations associated with exposure to various groups of allergens, levels of sensitization, severity of the disease, and the influence of previous and concomitant allergic and other somatic diseases.

In children with signs of atopy, upon contact with organic dust, microorganisms, aerosols of antibiotics, and enzymes, a combined development of atopic asthma and exogenous allergic alveolitis is observed. Such patients had high concentrations of total IgE in the blood serum.

The formation of BA in most cases occurs in early childhood, but is often recognized as a disease much later, and is most often regarded as obstructive bronchitis and bronchiolitis. Meanwhile, with a careful analysis of anamnestic and objective data in young children, asthma can be diagnosed in a timely manner. The presence in patients of a hereditary predisposition to allergies, manifestations of atopy (BP, AR), the connection between the occurrence of broncho-obstructive syndrome and allergenic exposure, the rapid reverse development of bronchial obstruction syndrome after the administration of bronchospasmolytic therapy, positive results of an allergological examination (increased levels of general and specific IgE in the blood serum, positive skin tests with allergens) give reason to consider the episodes of bronchial obstruction as a manifestation of asthma. It should be noted that intercurrent acute respiratory infections that often occur in such children, in turn, cause exacerbation of asthma.

AR is a common disease in children. According to epidemiological studies, up to 15% of the child population suffers from AR. AR in children in most reported cases is a manifestation of atopy. In 32 (48%) children, its occurrence is preceded by asthma and in 48 (72%) patients, asthma accompanies its course. Year-round AR, caused by sensitization to aeroallergens in homes, and seasonal AR, caused by sensitization to pollen, are currently considered as the leading risk factor for subsequent AD in such children. Evidence of the connection between the development of AR and atopy is the frequent detection of high levels of total IgE in the peripheral blood and blood of the nasal sinuses, the identification of elevated levels of specific IgE, and a family predisposition to allergic reactions and diseases. AR is often accompanied by involvement of the paranasal sinuses in the allergic process and the proliferation of adenoid vegetations. Occurring in children with asthma, AR aggravates the course of the latter. In pediatric practice, sometimes instead of a diagnosis of AR, a diagnosis of vasomotor rhinitis, manifested by sneezing, copious watery nasal discharge, and nasal congestion, is mistakenly made. These changes in vasomotor rhinitis are most often associated with disorders of the autonomic nervous system. It should be noted that an allergological examination performed for vasomotor rhinitis usually gives a negative result, whereas in children with AR it establishes the causal significance of certain allergens in the development of the disease. Hay fever in children is considered a classic manifestation of atopy. In children, hay fever most often manifests as AP, allergic conjunctivitis, asthma, and exacerbation of blood pressure. Most often, the development of hay fever is caused by sensitization to pollen from trees, cereals and weeds. When conducting an allergological examination, an increase in the level of total IgE is detected in 60 (89%) children with hay fever; in all patients, specific IgE antibodies to pollen allergens are detected. In 57 (85%) children with hay fever, a hereditary predisposition to allergic reactions and diseases is detected. There is a direct correlation between the level of sensitization to pollen allergens and the severity of the allergic process. It is important to identify this disease in the early stages, since early, before the development of polyvalent sensitization, allergen-specific immunotherapy can reverse the development of the disease and prevent the development of asthma.

Children often have combined manifestations of various allergic respiratory diseases - AR and BA, allergic faryngotracheitis and allergic bronchitis, allergic laryngotracheitis and BA. These combined clinical forms of allergic damage to the respiratory tract were previously designated as respiratory allergosis. Currently, the commonality of the mechanisms of development of AP, allergic bronchitis and BA is recognized and, in connection with this, some clinicians have proposed combining them into one nosological unit. It seems to us that this is inappropriate, since while the mechanisms of development of these diseases are similar, their differences in clinical manifestations and a certain difference in therapeutic approaches are obvious.

Among allergic diseases, there are diseases whose development is not associated with atopy, but IgE-mediated allergic reactions are leading in their pathogenesis. The emergence of such clinical forms of allergy is due to the development of sensitization to exogenous and endogenous allergens. Such a development mechanism in individual patients may underlie asthma, childhood eczema, AP, allergic urticaria, angioedema, gastrointestinal allergies, anaphylactic shock, toxicoderma, insect allergies, and some clinical forms of food and drug allergies.

The development of allergic diseases may be caused by other, non-IgE-mediated, allergic reactions. Immune complex reactions play a leading role in the development of such manifestations of drug allergies as serum sickness, vasculitis, thrombocytopenia, agranulocytosis, anemia, Arthus phenomenon, glomerulonephritis, and various types of exanthemas. Most often, their development is associated with the use of penicillin and other antibiotics, vaccines, serums, sulfonamides, anesthetics, and nonspecific anti-inflammatory drugs.

Cell-mediated allergic reactions leading to the development of allergic (immune) inflammation constitute the pathogenetic basis of the manifestations of drug allergies, which occur as contact and localized dermatitis. Cell-mediated immune complex reactions are also involved in the pathogenesis of acute toxic-allergic reactions. Rare manifestations of drug allergies include lupus erythematosus, the development of which is associated with autoimmune, immune complex and cell-mediated reactions.

Clinical observations indicate that children suffering from allergic diseases are susceptible to frequent acute respiratory diseases. More than 70% of children with allergic pathology suffer from 4 to 8 intercurrent acute respiratory diseases throughout the year, which gives grounds to classify them as a group of frequently ill children. In 44% of children with asthma and dermorespiratory syndrome, the first attack occurred against the background of an acute respiratory disease, and subsequent attacks of asthma in 56% of children were associated with intercurrent acute respiratory diseases.

Among the infectious agents that cause exacerbation of respiratory manifestations of allergies, the most often etiologically significant are the influenza virus and the RS virus - 79.74% and 82.56%, skin manifestations - parainfluenza and influenza - 37.27% and 28.26%. In the nasopharynx of children suffering from allergic diseases, persistence of parainfluenza viruses, influenza viruses, and adenoviruses is detected (27%, 58% and

84%). The long-term and massive persistence of various viruses in the child's body is one of the reasons for frequent respiratory morbidity in children with allergic pathology.

Children with allergic diseases have low levels of specific IgE antibodies to influenza and parainfluenza viruses. With recurrent respiratory and herpetic infections, there is a lack of mucosal immunity of the oropharynx in the form of a decrease in the content of secretory IgA, mainly due to inhibition of the synthesis of secretory IgA2.

The course of viral infections in children with allergic diseases is accompanied by an increase in the levels of general and specific IgE and sCD4+ in the blood serum, which indicates excessive antigenic stimulation and associated activation of humoral and cellular immunity.

The addition of acute respiratory infections of viral origin causes an increase in the production of IL4, IL5, IL8, TNF α and a decrease in IFN γ in the peripheral blood, indicating the development of disorders in the immune regulation system in children with allergic diseases.

There are no specific features in the clinical manifestations of allergic diseases in children who often suffer from acute respiratory diseases. Thus, viral infections in children are a common cause of exacerbations of allergic diseases and a subsequent increase in the level of sensitization. The results of the above studies do not give grounds to classify children with allergic diseases, who often suffer from acute respiratory diseases, as an independent clinical and pathogenetic variant of allergic pathology.

Allergic reactions and diseases are based on an immune mechanism of development. At the same time, there are clinical forms of non-allergic hypersensitivity that do not have immune mechanisms of development as their pathogenetic basis; until recently they were designated as pseudo-allergic reactions. European experts in allergy and clinical immunology in 2001 proposed a new classification of allergic reactions and diseases, in which pseudoallergic reactions are designated as "non-allergic hypersensitivity."

Most often, non-allergic hypersensitivity is manifested by urticaria, Quincke's edema, and various types of exanthemas. The development of non-allergic hypersensitivity is most often initiated by drugs, pharmacological agents used to diagnose certain diseases, and various chemical agents. The mechanism of development of non-allergic hypersensitivity may be different. A significant proportion of reactions caused by non-allergic hypersensitivity are associated with the direct release of histamine from mast cells and basophils, which occurs under the influence of a drug or other chemical agent introduced into the body. Direct release of histamine from mast cells can be caused by pharmacological agents such as blood substitutes, radiocontrast agents, anesthetics and muscle relaxants when administered intravenously. Reactions caused by non-allergic hypersensitivity, associated with an increased choice of histamine, are more often recorded in patients with allergic reactions and diseases.

Inactivation of histamine in the body is carried out by the enzyme diamine oxidase, as well as by methylation of the imidazole ring of histamine with the formation of methylimidazoleacetic acid, acetylation of histamine with the generation of

acetylhistamine and as a result of histaminopexy. Any disruption of histamine inactivation processes can contribute to the accumulation of histamine in the biological media of the body. Most often this occurs in diseases of the liver and kidneys. The combined effect of these factors creates additional conditions for the development of non-allergic hypersensitivity.

CONCLUSION

The development of non-allergic hypersensitivity reactions may be due to changes in the complement system that occur under the influence of pharmacological agents, manifested by activation of complement along the alternative pathway. Activation of the complement system through the alternative pathway through disruption of membrane permeability leads to mast cell degranulation and histamine release. This mechanism for the development of non-allergic hypersensitivity is observed with the administration of radiocontrast agents, anesthetics, and muscle relaxants. It is possible to develop non-allergic hypersensitivity due to activation of the synthesis of prostaglandins and leukotrienes by drugs. Such a mechanism may underlie bronchospasm, induced in some patients by nonspecific anti-inflammatory drugs.

The pathogenetic basis of non-allergic hypersensitivity may also be the effect of pharmacological agents on enzyme systems involved in the inactivation of serum kinins. Thus, radiocontrast agents have the ability to suppress the activity of carboxypeptidase, which may cause the accumulation of vasoactive peptides, which can cause pathological changes in the body.

Non-allergic hypersensitivity associated with the intake of food products is most often caused by the effects of chemical agents contained in them (preservatives, dyes, nitrates, nitrites, pesticides, increased amounts of histamine, tyramine, etc.). Its development is facilitated by concomitant disorders in the functioning of the digestive tract.

Factors contributing to the development of non-allergic hypersensitivity in some patients may cause exacerbation of true allergic diseases.

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