



Clinical and Pathogenetic Variants of Drug Allergy in Children

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Abstract: From the standpoint of modern clinical immunology, drug allergy (DA) is understood as clinically defined manifestations of allergy induced by certain drugs, while the pathogenetic basis of these manifestations is immunological mechanisms. Drug hypersensitivity reactions are detected in 5-10% of the population.

Key words: drug allergy, hypersensitivity, child.

Clinical manifestations of LA are characterized by great polymorphism. Currently, there is no generally accepted classification of aircraft. Previously, there was a proposal to subdivide the various clinical forms of LA depending on what type of immunopathological reactions was leading in the development of the clinical picture caused by LA lesions. Based on this, the following drug allergic manifestations were identified: 1) IgE-mediated LA; 2) cytotoxic reactions resulting from the interaction of a drug compound as a hapten with cell membranes, followed by the formation of antibodies to this complex; 3) immunocomplex reactions - the formation of immune complexes in this type of reaction leads to activation of the complement system, which leads to damage to cell membranes; 4) autoimmune reactions, the development of which is associated with the formation of autoantibodies to organs and tissues of the human body modified as a result of exposure to drugs; 5) drug allergic reactions, which are based on cell-mediated immunopathological reactions. Yu.P. Borodin proposed a clinical and pathogenetic classification of LA. According to this classification, it is proposed to distinguish two types of drug-induced allergic diseases (ADs). The first group consists of humoral-type ADs. These include systemic allergic reactions and diseases such as anaphylactic shock, acute urticaria and Quincke's edema, serum sickness and serum-like reactions, allergic bronchitis, bronchial asthma, allergic rhinitis, agranulocytosis, thrombocytopenic purpura. Allergy to drugs in this group of ADs can also manifest as exacerbation of the underlying AD - bronchial asthma, allergic bronchitis, chronic urticaria, atopic dermatitis. It is proposed to include local reactions in the form of the Arthus-Sakharov phenomenon in the group of ADs of humoral type of medicinal origin. According to this classification, the second group of ADs caused by drug sensitization includes cellular type ADs. It includes local allergic manifestations in the form of contact-type complications (contact dermatitis, dermatconjunctivitis, keratitis, etc.) and systemic ones: 1) fungal-like reactions (erythematovesicular dermatitis); 2) lupus-like syndrome; 3) complications of the hyperergic type (erythroderma, bullous and hemorrhagic dermatitis, Lyell's syndrome, Stevens-Johnson, etc.); 4) exacerbation of the underlying disease (some forms of eczema and dermatitis, vasculitis, periarteritis nodosa, etc.).

The first group of drug complications according to this classification is caused mainly by IgE-mediated allergic reactions (anaphylactic shock, urticaria, Quincke's edema, bronchial asthma, allergic bronchitis, atopic dermatitis); in the development of other diseases of this group, immune complex reactions can play a significant role (serum sickness, reactions such as the Arthus-Sakharov phenomenon and, finally, the occurrence of a number of them (agranulocytosis, thrombocytopenic purpura) can be a consequence of both cytotoxic and autoimmune reactions.



The participation of the cellular type of reactions in the development of the second group of diseases is obvious; at the same time, a certain role of the humoral component of immunity in their occurrence cannot be excluded. Most likely, in these clinical forms of LA, both humoral and cellular immunity are involved in their pathogenesis. Exposure to drugs can cause allergic damage to various organs and systems. In practical terms, it seems important to distinguish systemic lesions caused by sensitization to drugs and ADs of drug origin, associated primarily with damage to any particular organ and system.

A new classification of allergies, proposed in 2001 by EAACI (European Association of Allergists and Clinical Immunologists), proposes to distinguish drug hypersensitivity mediated by antibodies or LA lymphocytes and non-allergic drug hypersensitivity, previously called drug pseudoallergy. In turn, LA is divided into IgE-mediated and non-IgE-mediated. The presented classification has a more immunopathophysiological focus.

The issue of specific diagnosis of PA remains relevant and is currently not fully studied. This problem is closely related to the large variability of the immunopathological mechanisms of the development of LA, insufficient knowledge of drug metabolism, the nature and properties of medicinal haptens and their carriers in the body. Diagnosis of LA, due to the lack of a single universal technique that allows one to determine and analyze different types of immune response (humoral and cellular), must be comprehensive. Its implementation consists of a number of stages. First of all, a thorough and detailed collection of allergic and pharmacological history, a clinical examination of the patient, diagnostic reactions *in vivo* and, finally, allergy diagnostic tests *in vitro* are required.

Allergological history. A detailed allergy history is of great importance. On its basis, in some cases it is possible to quite clearly make the correct diagnosis. To establish a hereditary predisposition, a family allergy history is collected, in which the presence of AD and reactions in the parents and closest relatives of the child is determined. In this regard, great importance is attached to diseases such as bronchial asthma, atopic dermatitis, hay fever, allergic bronchitis, and, what is especially important, the presence of allergic reactions to drugs.

The presence of hereditary burden of AD and reactions on both lines (mother's line and father's line) is a high risk factor for the development of AD and reactions in the child.

Inflammatory diseases of viral and bacterial origin suffered by the mother during pregnancy often serve as a reason for prescribing antibacterial therapy. Currently, the possibility of intrauterine sensitization of the fetus by medicinal compounds passing through the placenta is considered proven.

Food allergy is a starting sensitization, on the basis of which a child's allergically altered reactivity, including sensitization to drugs, is easily formed.

Frequent and repeated acute respiratory viral infections, tonsillitis, bronchitis, and pneumonia also play an important role in the formation of pulmonary hypertension, since massive antibacterial therapy is often prescribed for them, which can cause sensitization to these drugs.

It is also mandatory to clarify the child's living conditions. A long stay in a damp apartment and a high degree of environmental humidity contribute to the development of fungal sensitization, against the background of which the risk of developing an allergy to penicillin antibiotics significantly increases due to the presence of common antigenic determinants in this group of antibiotics with fungal allergens.

Pharmacological history. When studying the causes of LA development, a number of points should be taken into account. The causative agents of many viral and other infectious diseases, as well as their toxins, metabolic and breakdown products, are strong antigens and can themselves cause the development of allergic reactions such as urticaria, various types of dermatitis, vasculitis, which can be mistakenly regarded as a consequence of the therapy. One should also take into account the fact that novocaine is often used as a drug solvent, which produces similar complications as the drug dissolved in it. When assessing drug complications that have arisen, the rate of occurrence of allergic



reactions, ADs that arose before the start of drug use, and the simultaneous use of other drugs are taken into account. It is known that taking antihistamines does not prevent the occurrence of drug allergic complications, while when taking glucocorticosteroids, LA usually does not occur. The method of drug administration, duration of treatment, dose, and repeated use of the same drug are also taken into account. Find out whether repeated similar reactions were observed when using the same drug. Drug-induced serum sickness, nephritis, and cytopenia develop more often with the use of high doses of drugs and longer therapy with them. Long courses of drug therapy increase the duration of exposure to the drug and increase the likelihood of developing an allergic reaction. The more often the medicine is used, the greater the likelihood of developing an allergic reaction. It is also known that delayed hypersensitivity occurs more often with local application of drugs. Allergic reactions develop more often with intramuscular use than with oral administration.

General pathogenetic and etiological principles for diagnosing drugs are identified.

The general principles of aircraft diagnostics are in the following:

- 1) exclusion of coincidence of the observed complication of drug therapy with the clinical picture of the underlying AD. Similar difficulties occur in patients with diseases such as bronchial asthma, atopic dermatitis, and allergic rhinitis. In these cases, an allergic reaction to the drug can be veiled by the picture of the underlying disease;
- 2) exclusion of the toxic effect of the drug.

The pathogenetic principles of diagnosing LA come down primarily to differential diagnosis of allergic and pseudoallergic reactions, as well as to the exclusion of the prostaglandin mechanism of complications, as, for example, in the case of the development of bronchospasm after taking acetylsalicylic acid and other nonspecific anti-inflammatory drugs.

The etiological principles of diagnosing LA are to determine the causally significant allergen (medicine), as a result of which an allergic reaction occurred.

Most often, the development of allergic reactions is observed with the use of penicillins, cephalosporins, muscle relaxants, anti-tuberculosis drugs, anticonvulsants, insulin, and enzymes.

There are a number of laboratory methods used to diagnose PA. All of them are based either on the properties of allergic antibodies circulating in the blood, or on the specific properties of sensitized cells. As a result, the results of cellular and serological tests are not always identical, which requires complex laboratory diagnostics.

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