

Инфекционная аллергия – старая проблема с новыми вызовами

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Infectious allergy – old problem with new challenges

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Аннотация

Проблема инфекционной аллергии в последние несколько лет стала чрезвычайно актуальной. Это связано с увеличением числа первичных пациентов с бронхиальной астмой или кожными высыпаниями, которые возникли после или во время вирусной инфекции. Бесспорным лидером таких инфекций является COVID-19. Несмотря на очевидность взаимосвязи вирусной инфекции и изменения реактивности организма, мало исследователей работает в этом направлении. В этой публикации мы обобщаем наше представление об иммунологическом взаимодействии вирус-хозяин.

Ключевые слова

Инфекционная аллергия, астма, крапивница.

The prevalence of allergy is growing throughout the world; according to World Health Organization's (WHO) data, every fourth person in the world suffers from an allergic disease [1]. In addition to allergy, autoallergic ("autoimmune") diseases, autoinflammatory diseases, as well as a number of somatic pathologies – atherosclerosis, COPD, cardiovascular diseases and etc. should be added to the list of diseases with altered (increased, decreased) immune reactivity to non-infectious and infectious pathogens. The altered immune reactivity is in essence an allergy according to its definition [2].

The problem of infectious allergy has become extremely relevant in the last few years. This is due to an increased number of primary patients with asthma or skin rashes that occurred during or after a viral infection. The undisputed leader of such infections is COVID-19. We observe such patients almost daily (Fig. 1).

Summary

The issue of infectious allergy has been increasingly relevant in the last few years due to a growing number of patients with asthma or skin rashes associated with viral infection, most prominent cause being COVID-19. Despite the link between viral infection and changes in immune reactivity of the organism being obvious, research on the topic has been scarce. In this publication, we summarize our understanding of the immunological virus-host interaction.

Keywords

Infectious allergy, asthma, urticaria.

A classic example of an infectious allergy is tuberculosis. The diagnosis of this type is based on allergological testing of a delayed reaction. These are intradermal tests with Mycobacterium tuberculosis antigens (Mantoux test or Diaskin test) and laboratory tests aimed at determining interferon γ (INF γ) IGRA tests (TSPOT or QuantiFERON Test) [3].

The interaction of viruses and the host can lead to various immunological phenomena (Fig. 2). The virus can induce immunodeficiency (AIDS in HIV infection), initiate tissue fibrosis (cirrhosis in viral hepatitis), induce tumor growth (papillomatosis and cervical cancer in human papillomavirus; Kaposi's sarcoma is caused by herpes virus type 8; Burkitt's lymphoma is associated with the Epstein-Barr virus).

Viruses may be associated with the development of hypersensitivity in humans. Moreover, the virus can act as an allergen – viral exanthemas and

urticarial rash on the skin. The virus can be a trigger and inducer of hyperreactivity in asthma. A striking example is respiratory syncytial virus. The virus may be a necessary co-factor in the development of the allergic process. For example, the development of DRESS syndrome is closely related to the persistence of herpes simplex virus type 6.

Viral infection can also induce autoimmune diseases. For example, the development of diabetes mellitus in children is associated with frequent respiratory infections, and Crohn's disease with norovirus.

Despite the obvious relationship between viral infection and changes in the reactivity of the organism, few researchers are working in this direction [4].

It is known that allergy diagnosis of tuberculosis has medical and commercial success. Some authors suggest using interferon-gamma release tests IGRA tests to diagnose other infections, for example, cytomegalovirus infection, Lyme disease, HIV infection, EBV infection, Chagas disease [3]. IGRA tests may be useful for assessing T cell response to SARS-CoV-2 virus [5].

In our opinion, it is necessary to initiate studies about the immunological interactions between the virus and the host, with special attention to the development of hypersensitivity and allergy. The key diseases in the field of infectious allergy are bronchial asthma and urticaria.

Bronchial asthma is a heterogeneous disease with different underlying pathologic processes. Recognizable demographic, clinical and/or pathophysiological clusters are often referred to as "asthma phenotypes" [6,7]. Over decades of asthma research, its various phenotypes and endotypes have been identified. Each of asthma phenotypes and endotypes has its own development mechanisms. In our view, basic classification of asthma was made by A.D. Ado and P.K. Bulatov (1969), supplemented by G.B. Fedoseev (1982) [8]. That asthma classification distinguished 10 clinical and pathogenetic variants: atopic, infectious-dependent, autoimmune, steroid-dependent, dysovarian, severe adrenergic imbalance, cholinergic, neuropsychic, aspirin-induced, physical exertion asthma. GINA (2023) identifies other major



Fig. 1. Dermatological lesions in COVID-19

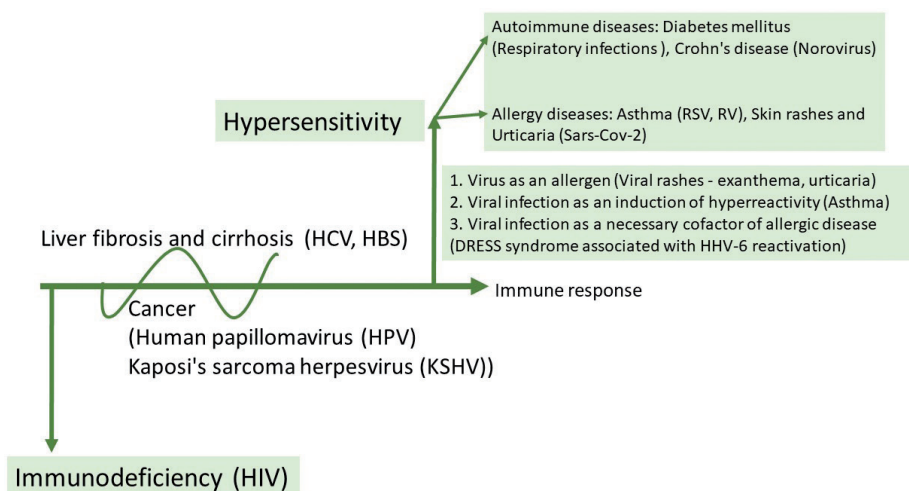


Fig. 2. Viral Immunomodulation

phenotypes as allergic, non-allergic, late-onset asthma, fixed airflow limitation asthma, and obese asthma.

According to the epidemiological studies, 75–80% of bronchial asthma exacerbations are associated with acute respiratory viral infections – respiratory syncytial viruses, rhinoviruses, coronaviruses, influenza viruses, etc. It is also reported that persistent intracellular infection, in particular viruses of the Herpesviridae family, are trigger factors, leading to increased bronchial hyperreactivity. Nevertheless if the diagnosis of the phenotype of allergic bronchial asthma associated with non-infectious aeroallergens has been developed, then the diagnosis of virus-induced or virus-associated asthma is currently difficult.

The mechanisms underlying the observed association between viral infection, allergic sensitization and the development of asthma are not fully understood. There may be a causal relationship in which viral infection induces various cellular factors that regulate host response, inflammation, airway repair and remodeling, and increased production of proinflammatory cytokines and chemokines [9]. Most likely, this mechanism plays a role in the development of both atopic and non-atopic bronchial asthma. Pathogenetic immune mechanisms, as well as methods of asthma immunodiagnosis depending on virus carriage, are not sufficiently developed at the moment.

A separate manifestation of infectious allergy are skin rashes that develop before or during a viral infection. Studies have been published on various skin symptoms in patients infected with SARS-CoV-2 [10]. 20.4% of patients with COVID-19 infection were diagnosed with an erythematous rash, diffuse urticaria and vesicular rashes similar to those of chickenpox [11]. Skin manifestations are caused by damage of small vessels walls in the dermis by circulating immune complexes in the form of deposits with infectious (viral) antigens.

Special forms associated with COVID-19 infection include urticaria, which may be a precursor to the onset of COVID-19 infection or occur along with its first symptoms. On the other hand, urticaria in COVID-19 infection may indicate a drug allergy and in this case refers to the clinical manifestation of toxicoderma. The acral location of blisters against the background of COVID-19 infection can also be attributed to the specific features of urticarial skin lesions in this viral disease [12].

Thus, infectious allergy represent a serious medical problem. Epidemiological studies are needed to reveal the prevalence of infectious-associated allergic diseases in different countries, followed by new standardized diagnostic methods and personalized therapy treatment.

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