SYNTROPIA OF ALLERGIC DISEASES

Navruzova Shakar Istamovna*; Ganieva Shakhzoda Shavkatovna**

*Professor,
Head of the department of Pediatrics,
Bukhara State Medical Institute, Bukhara city,
Republic of UZBEKISTAN
Email id: shakar.navruzova@gmail.com

**Associate Professor of the Department of Pediatrics,
Bukhara State Medical Institute, Bukhara city,
Republic of UZBEKISTAN
Email id: doctor.ganieva@gmail.com

DOI: 10.5958/2249-7137.2022.00030.1

ABSTRACT

The review article presents studies of foreign and domestic scientists devoted to the syntropy of allergic diseases - the formation of an ”atopic march". The authors analyzed the possibilities of predicting the development of allergic diseases and the need for further research to understand the processes of their progression.

KEYWORDS: *Atopicmarch, Allergy, Syntropy*

INTRODUCTION

Allergic diseases can successively replace each other in ontogenesis. In typical cases, a patient with atopy develops a spectrum of atopic diseases with age, defined as an "atopic march": in the first years of life, gastrointestinal and skin symptoms predominate, mainly caused by food allergens, later bronchial asthma (BA) and allergic rhinitis (AR) develop with sensitization to inhaled allergens **[1].**

For many allergic diseases, including BA, AR (pollinosis), atopic dermatitis (AtD) (eczema), food allergy, urticaria and others, comorbidity (syntropia) is characteristic. In clinical practice, a special form of syntropy is distinguished – the "atopic march", focusing on the consistent development of diseases caused by the production of IgE antibodies in response to environmental allergens, the onset of which occurs mainly in childhood **[2, 3].**

The first clinical manifestation of the "atopic march" in the overwhelming number of patients (86%) is eczema (atopic dermatitis). Approximately 20-30% of children with eczema have other allergies in subsequent years **[4].**

Among all children with several allergic manifestations, the largest group consists of children with eczema and asthma (38.3%), while the development of all three conditions, including eczema, asthma and allergic rhinitis, is not common and occurs only in 2.5% of patients with allergies **[5].** Concomitant clinical manifestation of allergopathologies significantly complicates therapeutic control, increases the need for glucocorticosteroids, therefore, to achieve optimal

effectiveness, combination therapy is necessary in accordance with the severity of each of the comorbid diseases **[6, 7].**

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 bronchi leads to 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 **[8, 9].**

The first link of the "atopic march" is often the ATD, against which a food allergy develops, which in the future, with uncontrolled flow and the influence of adverse factors, both external and internal, leads to the occurrence of BA, and then AR. Of course, the described path of the "atopic march" is only one of many different trajectories of development and variations in the progression of atopic diseases. A complete regression of atopy with age is also possible, the so-called "outgrowth" of the disease, which can be achieved in most patients only in the case of complete control over the disease with the achievement of stable remission and the appointment of maintenance therapy **[10].**

Despite this, it is the concept of the "atopic march" that is most often considered in clinical practice, since it is the most obvious way of developing allergic diseases as a result of the uncontrolled course of severe ATD in children. At the same time, it should be noted that the estimate of the prevalence of cases developing along the classical path of the "atopic march" may be overestimated. AtD is one of the most common inflammatory diseases of childhood, diagnosed in 15-25% of children and 4-7% of adults. Approximately half of all children suffering from severe ATD have food allergies to components of products such as cow's milk, eggs, wheat, soy, sesame and peanuts. According to epidemiological studies, food allergies are found in 6-10% of the world's population **[11, 12].**

According to a standardized epidemiological study within the framework of the ISAAC program (International Study of Asthma and Allergy in Childhood, international study of Asthma and Allergies in children), episodic wheezing was noted in 30% of children, persistent atopic asthma - in about 10% of children and 5% of adults. At the same time, the most frequent aeroallergens are house dust mites, pollen of trees and grasses, especially birch, wormwood and ragweed, mold fungi, as well as wool/dandruff of domestic animals **[13].**

In a population cohort study, HealthNuts recorded the frequency of food allergies in more than 5 thousand children at the age of 1 year and then at the age of 4 years. It was demonstrated that the prevalence of food allergy confirmed by a skin prick test decreased from 11% at the age of 1 year to 3.8% at the age of 4 years during the study period **[14].** At the same time, a survey of parents (using the standardized ISAAC questionnaire) showed that the prevalence of AD was 10.8%, symptoms of AD were observed in 16%, AR was detected in 8.3% of children. In the first 4 years of life, 50% of children from the study population experienced symptoms of various allergic diseases. R. Kapoor et al., studying the prevalence of the atopic triad in 2,270 children aged 2 to 17 years with a confirmed diagnosis of AtD, determined that 66% of the observed had

at least one additional form of atopy (BA or AR), while 38% of the studied patients had symptoms of both BA and AR. An association of allergic diseases with severe uncontrolled course of AtD was also revealed in these children **[15].** The manifestation of AtD in approximately 50% of children is observed in infancy (from 1 to 3 months), and in 30% of children aged 1 to 5 years. Pediatricians should pay attention to the first symptoms, because AtD is a significant risk factor for the development of other allergic diseases in children at an older age (in adolescence), first of all, it is the development of allergic rhinitis, bronchial asthma, the development of the "atopic march". **[16].**

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. The evidence of the relationship between AR and AD is primarily the results of numerous epidemiological studies: 30-40% of patients with AR have AD, and clinical manifestations of AR occur in more than 80% of patients with atopic AD. Patients with AR are three times more likely to develop AD compared to patients without AR. In more recent studies, which included questionnaires, lung function tests, provocative tests and skin tests, it was confirmed that AR is a high risk factor for the development of AD in children under 7 years of age, adolescents and adult patients. In more than 70% of adult patients, clinical manifestations of AR precede the manifestation of AD In preschool children, AR is often diagnosed after the diagnosis of AD, which certainly indicates a late diagnosis of AR [**17, 18].**

Late diagnosis, underestimation of the severity and untimely appointment of adequate therapy lead to the development of a number of complications, such as chronic sinusitis, otitis media, nasal polyposis. It was found that in 24% of children AR was a predisposing factor for the development of acute and chronic otitis media, and in 28% of cases – chronic rhinosinusitis **[19].**

Allergic rhinitis has been proven to be an independent risk factor for the development of bronchial asthma, increasing the chance of developing asthma by more than 3 times **[20].**

BA is a heterogeneous disease characterized by chronic inflammation of the respiratory tract, the presence of respiratory symptoms such as wheezing, shortness of breath, chest congestion and cough, which vary in time and intensity and manifest themselves together with variable airway obstruction. Bronchial asthma remains a global health problem affecting all age groups. Despite the fact that there is a decrease in the number of hospitalizations and deaths associated with AD, this disease still causes high damage to society and the healthcare system due to production losses, manifestations of family problems, and a decrease in the quality of life of patients **[21].**

Many researchers consider BA and AR as a single disease with a common mechanism of inflammation and a common genetic background ("one way, one disease, allergic rhinobronchitis"). A large number of clinical studies have shown that patients with AR have a 4-fold higher risk of developing AD. Patients with AR in 19-38% of cases suffer from AD, while about 80% of asthmatics are prone to rhinitis **[22].**

Hereditary predisposition is one of the risk factors for the development of the disease, however, the phenotypic realization of the genotype is due to the close relationship with the influence of

environmental factors. One of the triggering factors of the development of AD and the trigger mechanism of exacerbations are viral infections (rhinovirus, RS-viral, etc.), especially in children of the first 5 years of life. The effect of allergens, viruses and various nonspecific factors on the respiratory tract provokes the development of acute reactions in the sensitized organism in the form of edema of the bronchial wall, bronchospasm, hypersecretion, obstruction of the lumen by mucus. Chronic allergic inflammation eventually leads to structural changes in the bronchial wall (remodeling). Age-related features of the course of AD determine the main clinical manifestations of the disease and suggest appropriate approaches to diagnosis and treatment **[23].**

The frequency of association of allergic BA with AR is >80%. Allergic rhinitis is an independent risk factor for the development of AD, increasing the chance of getting AD by more than 3 times. AR allergic BA have the same etiological factors, and allergic inflammation in the nasal mucosa and inflammation in the mucosa of the lower respiratory tract also have more similarities than differences. The concept of the unity of the respiratory tract is based on the anatomical connection of the nose and lungs, the community of the respiratory epithelium, the presence of the nasobronchial reflex, which ultimately causes the same pathophysiological changes in the nasal and bronchial mucosa after provocation by a specific allergen **[24].**

Violation of the functions of the upper respiratory tract in AR, primarily respiratory and protective, inevitably leads to a violation of the functions of the lower respiratory tract, and the blockade of nasal breathing increases the contact of the lower respiratory tract with dry cold air and allergens. Therefore, it is natural that in the presence of AR symptoms in patients suffering from AD, the frequency of AD attacks, unplanned visits to the doctor, emergency calls, hospitalizations increases and the need for glucocorticosteroids (GCS) increases. In a study conducted in the UK, it was found that in patients with BA in combination with rhinitis, BA had an uncontrolled course 4-5 times more often than in patients with isolated BA **[25, 26].**

According to research results, the prevalence of AR in adult patients with AD varies from 24 to 94%, and the duration of the disease ranges from 50 to 100% in relation to life expectancy **[27].**

Many patients suffering from persistent AD have seasonal manifestations of AR, which significantly affect the course of AD and reduce the quality of life of patients **[28, 29].**

Sensitization to allergens through the inflamed skin of patients suffering from AtD can lead to allergic diseases that manifest in other organs, such as the gastrointestinal tract (food allergy), upper or lower respiratory tract (allergic rhinitis and bronchial asthma, respectively). These facts substantiate the concept of "unified airways", which demonstrates the close relationship between AR and BA and proves that the inflammatory response can be maintained and enhanced by interrelated mechanisms. Therefore, patients with AR should be examined for the presence of BA **[30,31].**

CONCLUSION

Currently, the issue of identifying the most significant risk factors affecting the implementation of BA and AR in children remains insufficiently studied, which must be taken into account when developing methods for forecasting and conducting individual preventive measures. The syntropy of allergic diseases along the path of the "atopic march" reveals the pathophysiological mechanisms of progression and makes it possible to predict the development of respiratory forms

of allergies in a child with atopic dermatitis in the future. **[32,33]** It is recommended to carefully analyze the anamnesis and take into account the aggravating factors of the development of atopic march that a particular child has in order to create an individual approach to the treatment and prevention of the development of other allergic diseases **[34].**

REFERENCES

1. Johansson SGO, Hourinehane JOB, Bousquet et al. A revised nomenclature for allergy. An EAACI position statement from the EAACI nomenclature task force. Allergy, 2016; 56:813-824

2. Dharmage SC, Lowe AJ, Matheson MC, Burgess JA, Allen KJ, Abramson MJ. Atopic dermatitis and the atopic march revisited. Allergy. 2014;69(1):17–27.

3. Spergel JM, Paller AS. Atopic dermatitis and the atopic march. J. Allergy Clin. Immunol. 2003;112(6):118–127.

4. Almqvist C, Li Q, Britton WJ, Kemp AS, Xuan W, Tovey ER, Marks GB. Early predictors for developing allergic disease and asthma: examining separate steps in the 'allergic march'. Clin. Exp. Allergy. 2007;37(9):1296–1302.

5. Punekar YS, Sheikh A. Establishing the sequential progression of multiple allergic diagnoses in a UK birth cohort using the General Practice Research Database. Clin. Exp. Allergy. 2009; 39(12):1889–1895.

6. Ivanova NA. Comorbidity of allergic rhinitis and bronchial asthma in children. Honey. advice. 2014;6:54–58.

7. Chernyak BA, Ivanov AF. Risk factors for exacerbations of bronchial asthma. Asthma and Allergy, 2017;(4):3-6

8. Braunstahl GJ, Kleinjan A, Overbeek SE, Prins JB, Hoogsteden HC, Fokkens WJ. Segmental bronchial provocation induces nasal inflammation in allergic rhinitis patients. Am J Respir Crit Care Med. 2000 Jun;161(6):2051-7.

9. Braunstahl GJ, Overbeek SE, Kleinjan A, Prins JB, Hoogsteden HC, Fokkens WJ. Nasal allergen provocation induces adhesion molecule expression and tissue eosinophilia in upper and lower airways. J Allergy ClinImmunol, 2019;107:469-476.

10. Zheng T, Yu J, Oh MH, Zhu Z. The Atopic March: Progression from Atopic Dermatitis to Allergic Rhinitis and Asthma. Allergy Asthma Immunol Res. 2011;3(2):67–73.

11. Aw M, Penn J, Gauvreau GM, et al. Atopic March: Collegium Internationale Allergologicum Update 2020. Int Arch Allergy Immunol. 2020;181(1):1–10.

12. Ganiyeva ShSh, Jurayeva FR, Hamdamova GR. (2021). Diagnostic Roleof Immunological And Biochemical Parametersin The Gastrointestinalfood Allergy In Children. Art of Medicine International Medical Scientific Journal, 2021;1(2):73–81.

13. Asher MI, Montefort S, Bjorksten B, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. Lancet. 2006;368(8537):733–743.

14. Peters RL, Koplin JJ, Gurrin LC, et al. The prevalence of food allergy and other allergic diseases in early childhood in a populationbased study: Health Nuts age 4-year follow-up. J Allergy Clin Immunol. 2017;140(1):145–153.

15. Kruglova LS, Gensler EM. Atopic dermatitis: new horizons of therapy. Medical Alphabet. Dermatology. 2019;1(7):29–32.

16. Sharova NM. Atopic march of treatment options for atopic dermatitis in young children. Medical Council, 2017;(19):205-207.

17. Leynaert B, Neukirch C, Kony S, Guenegou A, Bousquet J, Aubier M, Neukirch F. Association between asthma and rhinitis according toatopic sensitization in a population-based study. J Allergy ClinImmunol, 2014;113:86-93.

18. Rochat MK, Illi S, Ege MJ, Lau S, Keil T, Wahn U, Mutius EV. Germany Allergic rhinitis as a predictor for wheezing onset in school-aged children. J Allergy Clin Immunol, 2020;1170-1175

19. Bousquet J, Khaltaev N, Cruz AA et al. Allergic Rhinitis and its Impacton Asthma (ARIA) 2018 update. Allergy. 2018;63(86):8-160.

20. Shaaban R, Zureik M, Soussan D et al. Rhinitis and onset of asthma: longitudinal populationbased study. Lancet. 2018;372:1049-1057.

21. Nenasheva NM. Bronchial asthma and concomitant diseases: focus on allergic rhinitis. Lecheb. Case. 2014;(1):18–26.

22. Navruzova ShI, Khamrayeva DR. Regional Features of the Distribution of Chronic Constipation in Children. Eurasian Bulletin of Pediatrics. 2021;2(9):76-82.

23. Geppe NA, Kolosova NG. The value of modern guidelines in improving the monitoring and treatment of bronchial asthma in children (review). Bulletin of the Smolensk State Medical Academy, 2017;16(3):165-168.

24. Braunstahl GJ, Overbeek SE, Fokkens WJ, Kleinjan A, McEuen AR, Walls AF, et al. Segmental bronchoprovocation in allergic rhinitis patients affects mast cell and basophil numbers in nasal and bronchial mucosa. Am J Respir Crit Care Med 2001;164:858-65.

25. Bousquet J, Annesi-Maesano I, Carat F, Léger D, Rugina M, Pribil C, El Hasnaoui A, Chanal I. Characteristics of intermittent and persistent allergic rhinitis: DREAMS study group. Clin Exp Allergy. 2005 Jun;35(6):728-32.

26. Clatworthy J, Price D, Ryan D, Haughney J, Horne R. The value of self-report assessment of adherence, rhinitis and smoking in relation to asthma control. Prim Care Respir J. 2009 Dec;18(4):300-5.

27. Bousquet J, Van Cauwenberge P, Khaltaev N; Aria Workshop Group; World Health Organization. Allergic rhinitis and its impact on asthma. J Allergy Clin Immunol. 2001 Nov;108(5 Suppl):S147-334.

28. Ganieva ShSh, Radzhabova GB. Clinical and Laboratory Evaluation of the Health of Patients with Chronic Obstructive Pulmonary Disease Who Had Coronavirus Infection. CAJMNS

[Internet]. 2021 Oct. 18 [cited 2021Oct.28]; 76-0. Available from: http://cajmns.centralasianstudies.org/index.php/CAJMNS/article/view/353

29. Chernyak BA, Vorozhaeva II. Comorbid diseases in allergic rhinitis. Asthma and allergies. 2017;(1):3–7.

30. Kurbacheva OM, Polner SA, Smirnov DS. allergic rhinitis. An eternal problem and its modern solution. Medical Council, 2015;(3):84-91.

31. Ganiyeva ShSh, Rustamov BB, Panoyev XSh. Regional features of the frequency and clinic of respiratory allergy. New Day in Medicine. 2021;3(35):194-197.

32. Irvine AD, Mina-Osorio P. Disease trajectories in childhood atopic dermatitis: an update and practitioner's guide. Br J Dermatol. 2019;181(5):895–906.

33. Loh W, Tang M. The Epidemiology of Food Allergy in the Global Context. Int J Environ Res Public Health. 2018;15(9):2043.

34. Giyasovna YG, Ramazanovna BN, Samiyevich BS. Statistical Analysis of The Structure of The Birth Rate of Underweight Children in The Bukhara Region. Art of Medicine International Medical Scientific Journal, 2021;1(2):73–81.