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THE INFLUENCE OF ATOPY ON CYSTIC FIBROSIS COURSE IN CHILDREN

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Introduction. The modern medicine space dictates to us new searching rules for the key link in the disease pathogenesis. The science development shows us that most pathological conditions can have a large number of course options, since the number of disease phenotypes depends on many modifying factors. And even those diseases that we consider congenital and their course is already genetically predetermined, they can have very different course options, depending on the presence of other modifying factors.

The two simultaneously relevant conditions that interested us in this study are cystic fibrosis (CF) and atopy.

Cystic fibrosis is one of the most common hereditary diseases with variety of clinical manifestation [1]. CF course depends on not only difference of CF transmembrane conductance regulator gene mutations, but also on other modifiers that affect the phenotype of the disease [2, 3]. In turn, atopy is a predisposition to the development of allergic diseases with the development of increased immunoglobulin E (IgE) production and other immune status indexes [4]. This condition is also classified as congenital and one of the modifiers of CF course [5].

Therefore, studying the peculiarities of the cystic fibrosis course in children with atopy in the Kharkiv region will help to expand theoretical knowledge about the features of the cystic fibrosis phenotype associated with atopy. The received information can be used to improve treatment algorithms for patients with CF and prevent the development of disease complications.

The purpose of the study: to improve medical care for patients with CF by clarifying the pathogenetic role of atopy in the disease course.

Materials and methods. The research was conducted in the pulmonology department of the Kharkiv Regional Clinical Children’s Hospital No 1. Clinical and paraclinical examinations of patient with CF were carried out according to the unified clinical protocols. Forty-two children with CF were observed. The peculiarities of children with CF and atopy were evaluated in comparison with patients with CF without atopy. The control group (for assessment of immune status) consisted of 30 practically healthy children who had been randomized to the age.

Immune status assessment was carried out by using of the standard methods in the remission period. The determination of the total Ig E in serum was carried out by solid phase enzyme-linked immunosorbent assay (ELISA). The determination of the specific IgE to Aspergillus fumigatus was carried out by ELISA with fluorescent label.

The study was conducted with respect to human rights in accordance with the legislation in force in Ukraine, in compliance with international ethical requirements and didn’t violate ethical norms in science and standards for conducting biomedical research.

The results were processed by the IBM SPSS Statistics program according to the methods of variance statistics. Statistical significance was the difference between the indicators at $p < 0.05$.

Results. Forty-two children were examined. Diagnosis of CF was based on clinical and paraclinical characteristics and confirmed by the results of pilocarpine test. The boys were predominant among the examined patients (66.7%). According to age, the majority were children of the senior school age (Table 1).

Table 1

Distribution of children with cystic fibrosis by gender and age

Age / Gender	1 year – 2 years 11 months 29 days		3 years – 6 years 11 months 29 days		7 years – 11 years 11 months 29 days		12 years – 17 years 11 months 29 days		Total	
Number	n	%	n	%	n	%	n	%	n	%
Boys	4	80	3	50	12	85.7	9	52.9	28	66.7
Girls	1	20	3	50	2	14.3	8	47.1	14	33.3
Total, n	5		6		14		17		42	

Determination of the total IgE level showed that 19 patients (45.2%) had elevated levels and 23 patients (54.8%) had results of the total serum IgE within the age range. The mean value of the total serum IgE was 344.6 (63.8; 670.3) IU / ml. Allergic rhinitis was detected in 9.6% of patients, 2.4% of patients had bronchial asthma.

In the group with elevated and normal levels of total serum IgE, boys were predominant, as in the general population, and accounted for 73.6% and 60.8%, respectively ($p > 0.05$).

The first manifestations of CF were represented mainly by intestinal signs in both groups at 68.4% and 73.9% of cases, respectively ($p > 0.05$, table 2).

Table 2

Cystic fibrosis manifestation depending on the presence of atopy

CF manifestation signs / Group	Intestinal		Respiratory	
	n	%	n	%
Atopy (n=19)	13	68.4	6	31.6
Norm (n=23)	17	73.9	6	26.1

Manifestations of intestinal symptoms in the group with elevated total IgE in 42.0% of cases were found in the newborn period and in 58.0% of cases were found in the infant period. Manifestations of these symptoms in the group with normal level of total IgE were found later: in 17.0% of cases – in the newborn period, 57.0% – the infant period, 22.0% – the toddler period, 4.0% – the preschool period.

Data analysis of the clinical features of CF course in children with elevated level of IgE (severity of lung and liver lesions) revealed a results without significant differences between groups. This fact may be due to small number of CF patients in the Kharkov region.

Level of A. fumigatus specific IgE was determined in the group with elevated level of total IgE (n = 19). It was at 0.12 (0.10; 0.48) IU/ml level. Among these patients, 15.78% of children had a high level of antibodies to A. fumigatus, and 68.48% – very low level of A. fumigatus specific IgE.

Predominance within respiratory pathological microorganisms in sputum – S. aureus, Klebsiela pneumoniae, C. albicans; in the mucous membrane of the throat and nose – Klebsiela pneumoniae were found in group with elevated level of total IgE ($p < 0.05$).

To assess the level of sensitization to different group (n = 50, food, domestic, pollen groups of allergens) in patients with an elevated level of total IgE was conducted skin prick testing. Investigation was provided in condition of compliance with the sick child and his parents, n = 13). Very sensitive reaction to dandelion was established is 7.69%; moderately sensitive – to ragweed (23.07%, cat’s wool 7.69%, house dust 7.69%, dandelion 7.69%; mildly sensitive – to house dust 38.46%, cocoa 30.79%, orange 23.07%, pillow feathers 15.38%, cat’s wool 15.38%, egg white 15.38%, chicken meat 15.38%, lemon 15.38%, cabbage 15.38%, sunflower 15.38%, timothy 15.38%, plantain 15.38%, foxtail 15.38%, dandelions 15.38%, apple 7.69%, tangerine 7.69%, buckwheat 7.69%, birch 7.69%, ragweed 7.69%.

The immunological indicators of patients in the group with atopy were analyzed in comparison with CF patients with a normal level of total IgE. Patients with CF and atopy were found to have a probable increase in the levels of CD3, IgM, spontaneous NBT; phagocytosis of latex; decreasing in the levels of CD4, IgA compared to the group with a normal level of total IgE.

Discussion. The CF and atopy issue has been around for a very long time, dating back to 1949 when Lowe C.U. first reported increased atopy prevalence among patients with CF [6, 7]. There is still no definitive data on the complete characterization of the CF phenotype associated with atopy. Every year, new and updated data appear on the clinical and para clinical characteristics of patients with CF and atopy. Scientists express the opinion that such a variable picture is represented by the fact that so far the authors, assessing various indicators of atopy in CF patients, have not found a common final and clear decision about the role of their influence on the course of the disease [6].

There is evidence, that atopy can affect the occurrence of concomitant conditions, such as asthma, allergic bronchopulmonary aspergillosis (ABPA) and worsen the severity of CF [5]. Allergic inflammation of the bronchi and viscous mucus contribute to the colonization of the respiratory tract by pathogenic microorganisms [8]. These patients need prolonged courses of antibiotics which increased risk of allergic sensitization, particularly in the presence of family history of atopy.

The allergic sensitization to Aspergillus fumigatus precedes the development of ABPA, which occurs in up to 10% of patients with CF [5]. The main allergic reactions in patients with CF are reactions caused by sensitization to Aspergillus fumigatus. However, recent studies have shown that the level of sensitivity to ordinary domestic and pollen allergens

increases with the age [9]. We didn’t find that during out study high level of sensitivity to ordinary domestic, food and pollen allergens in children with CF.

Among patients with CF, allergic rhinosinusitis is common, which causes severe anatomical changes in the nasal cavity. It is often underestimated against the background of the severity of lung disease [10, 11].

According to the hygienic hypothesis of the development of allergic diseases, in the pathogenesis of infectious inflammation the main role is taken by Th1 cells, and in the pathogenesis of allergic inflammation the main role is taken by Th2 cells [12]. The mechanism of interaction between these two units is unclear in patients with CF and potent lifelong infectious process.

Therefore, the characteristics of the CF phenotype associated with atopy are a relevant and incompletely studied issue today. Further study of this issue will help expand data on the characteristics of the CF course depending on the influence of other modifying factors, which will improve the therapeutic procedures individualization in the treatment of patients with CF, reduce the incidence of complications and economic costs for the treatment of severe conditions, and improve the life quality of this category patients.

Conclusion. Features of the CF phenotype associated with the atopy were analyzed. Early manifestation of the CF with intestinal symptoms, prevalence in bacteriological tests of S. aureus, Klebsiela pneumoniae, C. albicans, increased levels of CD3, IgM, spontaneous NBT; phagocytosis of latex, decreasing in the levels of CD4, IgA were found in children with CF and atopy.

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SUMMARY

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The relevance of research. The course of cystic fibrosis (CF) depends on the influence of different modifying factors. One of these factors is atopy. The role of atopy in CF course is incompletely determined today and requires further study.

The purpose of the study: to improve medical care for patients with CF by clarifying the pathogenetic role of atopy in the disease course.

Materials and methods. Analysis of data from a clinical and paraclinical examination of 42 children with CF in the Kharkiv region. Patients were divided into two groups: with an elevated level of total immu-

noglobulin E (n=19) and with a normal level of this indicator (n=23) to determine the features of CF course depending on the atopy presence.

Results and discussion. In the group with elevated and normal levels of total serum IgE, boys were predominant, as in the general population, and accounted for 73.6% and 60.8%, respectively. The first manifestations of CF were represented mainly by intestinal signs in both groups at 68.4% and 73.9% of cases, respectively. Data analysis of the clinical features of CF course in children with elevated level of IgE (severity of lung and liver lesions) revealed results without significant differences between groups. High level of sensitivity to ordinary domestic, food and pollen allergens was not detected in children of group with elevated level of IgE. Patients with CF and atopy were found to have a probable increase in the levels of CD3, IgM, spontaneous NBT; phagocytosis of latex; decreasing in the levels of CD4, IgA compared to the group with a normal level of total IgE.

Conclusion. Features of the CF phenotype associated with the atopy were analyzed. The received data can be used when determining the treatment algorithm, taking into account the individual characteristics of the disease course.

Key words: children, cystic fibrosis, modifying factors, atopy.

РЕЗЮМЕ

ВПЛИВ АТОПІЇ НА ПЕРЕБІГ МУКОВІСЦИДОЗУ У ДІТЕЙ

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Актуальність. Перебіг муковісцидозу (МВ) залежить від впливу багатьох модифікуючих факторів. Одним із таких факторів є атопія, роль якої у перебігу МВ визначено неостаточно на сьогоднішній день, та потребує подальшого вивчення.

Мета: удосконалення медичної допомоги хворим на МВ за допомогою визначення патогенетичної ролі атопії у перебігу захворювання.

Матеріали та методи. Аналіз даних клініко-параклічного дослідження 42 дітей, хворих на МВ, у Харківському регіоні. Для визначення особливостей перебігу МВ залежно від наявності атопії, хворих було розподілено на дві групи: з підвищеним рівнем загального імуноглобуліну Е (n=19) та з нормальним рівнем даного показника (n=23).

Результати та обговорення. У групі з підвищеним і нормальним рівнем загального IgE, як і в загальній популяції, переважали хлопчики – 73,6% і 60,8% відповідно. Маніфестація МВ була представлена здебільшого кишковими ознаками в обох групах у 68,4% та 73,9% випадків відповідно. Аналіз даних клінічних особливостей перебігу МВ у дітей з підвищеним рівнем IgE (тяжкість ураження легень і печінки) виявив результати без достовірних відмінностей між групами, на що, вірогідно, вплинула малочисельність груп дослідження. У дітей групи з підвищеним рівнем IgE не виявлено високого рівня чутливості до звичайних побутових, харчових та пилкових алергенів. У хворих на МВ та атопію виявлено вірогідне підвищення рівня таких показників, як CD3, IgM, НСТ спонтанний; фагоцитоз з латексом; зниження рівнів показників CD4, IgA порівняно з групою з нормальним рівнем загального IgE.

Висновок. Вивчено особливості фенотипу МВ, що асоційований з атопією. Отримані дані можуть бути використані при призначенні алгоритму лікування з урахуванням індивідуальних особливостей перебігу захворювання.

Ключові слова: діти, муковісцидоз, модифікуючі фактори, атопія.

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