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POSSIBILITY OF SWITCHING OF A BIOLOGICAL DRUG WHEN TREATING CHILDHOOD ASTHMA (A CLINICAL CASE)

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Introduction. Genetically engineered biological drugs (GEBD) are widely used in the treatment of children with uncontrolled bronchial asthma (BA). In Russia, several GEBD have been registered for the treatment of children and adolescents with asthma, including anti-immunoglobulin E/anti-IgE (omalizumab), anti-interleukin 5/anti-IL-5Ra (mepolizumab), and anti-IL-4Ra (dupilumab). The choice of GEBD depends on the BA phenotype and genotype. However, in pediatric practice, the difficulty of determining a BA endotype complicates the search for an effective drug. For this reason, there is a possibility of insufficient effectiveness of the recommended expensive therapy and the need to revise the treatment of GEBD in accordance with the phenotypic features of the disease.
Clinical case description. The paper presents a dynamic follow-up of a 7-year-old child with severe asthma and concomitant atopic dermatitis (AD) receiving GEBD therapy. The initial biological drug was omalizumab. Subsequently, due to insufficient control of the symptoms of the disease and exacerbation of severe atopic dermatitis, a switch to dupilumab was performed. The change in GEBD contributed to achieving control over BA symptoms and a relief of the skin condition.
Conclusions. Our observation shows the effectiveness and safety of switching between omalizumab to dupilumab in children with severe asthma and concomitant AD. Further research is needed to clarify the clinical profile of patients in order to determine predictors of an effective choice of biotherapy and resolve the issue of switching to various monoclonal antibodies.

Keywords: bronchial asthma; atopic dermatitis; Type 2 inflammation; genetically engineered biological drugs; omalizumab; dupilumab; children

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ВОЗМОЖНОСТИ ПЕРЕКЛЮЧЕНИЯ БИОЛОГИЧЕСКОГО ПРЕПАРАТА ПРИ ЛЕЧЕНИИ БРОНХИАЛЬНОЙ АСТМЫ У ДЕТЕЙ. КЛИНИЧЕСКОЕ НАБЛЮДЕНИЕ

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Введение. В терапии детей с неконтролируемой бронхиальной астмой (БА) активно используются генно-инженерные биологические препараты (ГИБП). В России для лечения детей и подростков с БА зарегистрировано несколько ГИБП: антииммуноглобулин Е (IgE) (омализумаб), антиинтерлейкин 5 (IL-5/анти-IL-5Rα) (Меполизумаб®) и анти-IL-4Rα (Дупилумаб®). Выбор ГИБП зависит от фенотипа и эндотипа БА. Однако в педиатрической практике определение эндотипа БА затруднительно, в связи с чем поиск эффективного препарата остается непростой задачей. По этой причине существует вероятность недостаточной эффективности рекомендованной дорогостоящей терапии и необходимости пересмотра лечения ГИБП в соответствии с фенотипическими особенностями заболевания.
Описание клинического случая. В работе представлено динамическое наблюдение за ребенком 7 лет с тяжелым течением БА и сопутствующим атопическим дерматитом (АтД), получающим в терапии ГИБП. Исходным биологическим препаратом был омализумаб. В последующем в связи с недостаточным контролем симптомов заболевания и обострением тяжелого атопического дерматита проведено переключение на Дупилумаб®. Смена ГИБП способствовала достижению контроля симптомов БА и купированию кожного синдрома.
Выводы. Наше наблюдение показывает эффективность и безопасность переключения с биологического препарата омализумаб на препарат Дупилумаб® у детей с тяжелым течением БА и сопутствующим АтД. Необходимы дальнейшие исследования для уточнения клинического профиля пациентов с целью определения предикторов эффективного выбора биологической терапии и решения вопроса о переходе на различные моноклональные антитела.

Ключевые слова: бронхиальная астма; атопический дерматит; Т2-воспаление; генно-инженерные биологические препараты; омализумаб; Дупилумаб®; дети

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INTRODUCTION

Bronchial asthma (BA) is a chronic heterogeneous respiratory disease with the incidence of about 400 million people worldwide[1]. In Russia, according to the results of epidemiological studies, 6.9% of adults and about 10% of children and adolescents suffer from BA[2].

Currently, BA treatment is aimed at achieving control over the symptoms of the disease and preventing exacerbations. Anti-inflammatory drugs form the basis of controlled drug therapy; however, BA therapy is selected individually according to the phenotype and age of the patient. The treatment volume increases or decreases depending on the controllability of the symptoms of the disease. According to the recommendations of the Global Initiative for Asthma (GINA), inhalant glucocorticosteroids (ICS) are a basic therapy in children under five years of age, while combined drugs — fixed combinations of ICS with long-acting β2-agonists (LABA) — can be used starting from the age of six-year-olds. In addition, from two years of age, antileukotrienes (leukotrienes receptor antagonists, LTRAs) are recommended as a baseline therapy. Provided high adherence and proper inhalation technique, the majority of patients (80%) respond positively to such a therapy with the achievement of symptom control. However, 5–10% of patients are resistant to standard therapy, having a high rate of BA exacerbations and emergency treatment [1]. Currently, the drugs of choice for this patient group are genetically engineered biological drugs (GEBD), which are selected based on the phenotype and endotype of the disease [1].

The BA phenotype is a combination of features that describes clinical differences between patient groups and largely determines the BA clinical outcomes. There are five main BA phenotypes in adults, i.e., allergic, non-allergic, with late onset, with fixed airway obstruction, and BA in obese patients [1, 2]. The allergic (atopic) BA phenotype is most common in pediatric practice. This phenotype is associated with a family history of atopic diseases, early onset in childhood, the presence of concomitant allergic diseases in the patient (allergic rhinitis, pollinosis, atopic dermatitis (AD)), being characterized by severe sensitization to allergens [1].

The BA endotype is a disease subtype characterized by a unique pathogenetic or molecular mechanism. One BA endotype may underlie several phenotypes [1–4]. There are two most common BA endotypes, i.e., with the dominance of T2 inflammation (T2-BA) and without it — non-T2-BA, and a mixed endotype. As a rule, non-T2-BA is characterized by neutrophilic or paucigranulocytic inflammation, whereas T2-BA is characterized by the presence of eosinophilic inflammation of the respiratory tract [4]. Eosinophilic inflammation in T2-BA is formed due to the involvement of Th2 lymphocytes and type 2 innate lymphoid cells (ILC 2), which produce excess T2-profile cytokines IL-4, -5, -13. The secretion of these cytokines triggers IgE-related hypersensitivity reactions in the lower respiratory tract, activating and maintaining the inflammatory process. The markers of the BA T2-endotype include an increase in immunoglobulin E (IgE) in blood serum, the eosinophil blood level >150 cells/μL and/or the number of sputum eosinophils >2%, and/or the level of nitric oxide in exhaled air (FeNO) >20 particles per billion (ppb) [3].

The above inflammatory endotypes served as a theoretical basis for the development of personalized approaches to BA therapy. In this regard, the creation of GEBD is a promising direction. The GEBD mode of action consists in binding to a certain determinant, e.g., a cytokine or a receptor, and blocking the further inflammatory process. Due to this selectivity, biologics are ideally suited for personalized or targeted medicine.

In Russia, three GEBD are currently used for BA treatment in pediatric practice. Among them are anti-immunoglobulin E/anti-IgE (omalizumab), anti-interleukin-5/anti-IL-5Ra (mepolizumab), and anti-IL-4Ra (dupilumab) [3]. These drugs have demonstrated their efficacy in BA treatment in clinical trials. In the setting of GEBD therapy, most patients showed a decreased relapse rate, improved BA control and lung function [5–7]. However, the effectiveness of therapy is largely determined by the correct choice of GEBD, which is based on the assessment of the patient's BA phenotype and BA endotype. In pediatric practice, the determination of the endotype and related biomarkers may be problematic. Thus, children with eosinophilic BA may not exhibit an increase in all markers of T2 inflammation, similar to adult patients. BA patients may be phenotypically similar, but have different responses to GEBD. This results in significant difficulties in selecting GEBD and their insufficient effectiveness in actual clinical practice [3, 5]. Thus, according to [8], about 10% of patients treated with GEBD experienced insufficient clinical response during therapy. In such cases, experts recommend considering changing the drug and switching to another monoclonal antibody [1]. Unfortunately, there are currently no clear clinical criteria for selecting the most effective biological drug, as well as evidence-based recommendations regarding the timing of the transition from one biological drug to another [9]. Switching to another biological drug is possible in case of insufficient control of BA during therapy, the presence of potential adverse events (hypereosinophilia, for example), and emergence of concomitant pathology (nasal polyps, AD) [1].

Omalizumab was the first monoclonal antibody (mAb) approved as an adjunctive therapy for patients with severe persistent allergic BA. It is a recombinant humanized IgG1 mAb that inhibits the binding of freely circulating IgE to the high-affinity IgE receptor (FcεRI) on the surface of both mast cells and basophils, thereby limiting the release degree of allergic reaction mediators. The omalizumab effectiveness in patients who responded to treatment is due to its inhibitory effect on the type 2 cytokines (IL-4, IL-5, and IL-13) release and eosinophil transport.

Numerous studies performed in different countries, including the Russian Federation, have shown the effectiveness of omalizumab in the treatment of adults and children >6 years of age with severe and moderate atopic BA, uncontrolled by high doses of ICS in combination with LABA [10, 11]. The atopic nature of BA must be proven

[1] GINA. Global Strategy for Asthma Management and Prevention. Global Initiative for Asthma, 2024.
[2] Bronchial asthma. Clinical practice guideline. Ministry of Health of Russia; 2024.

by significant sensitization (positive skin tests and/or the presence of specific IgE antibodies) to allergens. Total serum IgE should range within 30–1500 IU/mL in adults and children >12 years of age and 30–1300 IU/mL in children over six years of age. Omalizumab is administered subcutaneously at a dose of 150–375 mg every two or four weeks. The dosage and frequency are calculated based on the body weight and the total serum IgE level. The first evaluation of the effectiveness of omalizumab treatment is recommended after 16 weeks of treatment[3]. After this follow-up period, treatment may be discontinued due to a lack of efficacy.

Since the approval of omalizumab, a number of randomized clinical trials (RCTs) have demonstrated the therapeutic efficacy of subcutaneous administration of omalizumab [10, 12]. According to the literature [13], the highest therapy was observed in patients with sensitization to allergens. In a combined analysis of data from five RCTs, including 2236 patients with moderate and severe persistent allergic BA who received ICS in moderate and high doses, improved clinical outcomes during omalizumab treatment were associated with a decreased peripheral blood eosinophil count, while the worst clinical outcomes were associated with an increased peripheral blood eosinophil count [14].

The researchers in [15] obtained the data indicating the possibility of switching from omalizumab to other biological drugs (mepolizumab, dupilumab) with insufficient control of BA symptoms (for example, in patients with a high level of eosinophilic inflammation). However, there are no clear clinical criteria and biological markers to identify patients in whom such a drug switch will be effective.

Dupilumab is a human monoclonal antibody capable of inhibiting IL-4 and IL-13 signaling by specifically binding to their common IL-4R receptor component. IL-4 and IL-13 are the key factors in T2 inflammation, which plays an important role in the pathogenesis of many atopic diseases. Dupilumab may be recommended for children (with BA) ≥12 years of age. According to research data, the drug effectiveness has been proven in patients with increased eosinophil count and FeNO (i.e. ≥150 cells/μL and ≥25 ppb, respectively). It is important to note that dupilumab is the only effective GEBD in children with AD.

A sufficient number of clinical studies have confirmed the feasibility of applying dupilumab in BA treatment. In case of insufficient efficiency, it is recommended to switch to another GEBD.

Mepolizumab is a humanized monoclonal antibody (IgG1k) directed against human IL-5 and preventing its interaction with a specific receptor on the surface of eosinophils, initiating recovery of the IL-5-dependent eosinophil count to the physiological norm. Mepolizumab is indicated for children ≥6 years of age as an additional supportive therapy for severe BA with an eosinophilic profile of respiratory tract inflammation[4].

The GINA report also lists additional indications for the choice of GEBD. In addition to BA, mepolizumab has indications as a nasal polyposis and eosinophilic granulomatosis with polyangiitis (from the age of 18); omalizumab has indications as a chronic idiopathic urticaria (from the age of 12) and nasal polyposis (from the age of 18); mepolizumab has chronic rhinosinusitis with nasal polyposis (from the age of 18), eosinophilic esophagitis (from 12 years old) and moderate to severe AD with insufficient response to therapy with topical medications (from six months), which is especially important given the comorbidity in BA.

Thus, the choice of GEBD is a difficult task in clinical practice. The effectiveness of biotherapy depends on the correct assessment of the patient's clinical, anamnestic, laboratory, and instrumental data. An effective biological drug can only be selected based on a comprehensive assessment of the initial data based on determination of the BA phenotype and the expected BA endotype. At the same time, the insufficient effect of GEBD therapy and the appearance of concomitant pathologies is a reason for reassessing the patient's data followed by a possible decision to switch to another GEBD.

In this article, we present a clinical case of a patient with severe BA, who underwent a change of GIBT due to a worsening of the disease course and an AD exacerbation.

CLINICAL CASE DESCRIPTION

The 7-year-old patient was observed during the 2020–2024 period at the Federal Scientific and Clinical Center for Children and Adolescents. The child had been admitted with complaints of recurrent bronchial obstruction syndrome, persistent cough, and nasal congestion for a one year.

It became known from the patient's life history that the girl was born from the second physiological pregnancy, the second spontaneous vaginal delivery at term. The birth body length was 52 cm; birth weight was 3150 g. The Apgar score was 8/9. She was breastfed on the first day and was breastfed for up to 5.5 months. She grew and developed according to her age. She was vaccinated according to the National Calendar of Preventive Vaccinations. The hereditary history of allergic diseases was burdened: the maternal brother and maternal uncle suffered from hay fever, allergic rhinoconjunctivitis; the paternal grandmother suffered from asthma.

At the age of six months, skin rashes appeared after the introduction of complementary foods and the transfer to a milk formula. The skin process was widespread, located on the face, trunk, and limbs. The child was diagnosed with atopic dermatitis. Against the background of therapy with topical corticosteroids (TCS) and moisturizers, relief of the skin syndrome with positive age dynamics was noted. By the age of 1.5 years, the skin process was limited.

From the age of two, complaints of nasal congestion, rhinorrhea, and itchy eyes in the spring appeared. Constant nasal congestion was noted throughout the year. The examination revealed significant sensitization to pollen (birch, weeds), household (dust mites), and epidermal allergens (cat epithelium). Second-generation

[3] Xolair® (omalizumab) patient information leaflet. https://grls.rosminzdrav.ru/Grls_View_v2.aspx?routingGuid=2ace7eaa-ac77-48e5-9571-529dc017235a
[4] Nucala® (mepolizumab) patient information leaflet. https://grls.rosminzdrav.ru/Grls_View_v2.aspx?routingGuid=b7a6f6cf-2e9c-4718-91c9-442c9c294777

systemic antihistamines and intranasal corticosteroids were recommended for drug therapy, which significantly improved the patient's quality of life.

The first episode of bronchial obstruction was noted at the age of 2.5 years after contact with a cat. Subsequently, episodes of bronchial obstruction recurred 1–2 times a month against the background of acute respiratory viral infections, contact with animals. In the spring and summer periods, the episodes were observed almost daily. At the age of three, the child was diagnosed with BA followed by prescription of low doses of ICS (budesonide 250 μg/day via a nebulizer) as a control therapy. Subsequently, there were complaints of bouts of bronchial obstruction during physical exertion. LTRA (montelukast 4 mg/day) were added in the therapy. During therapy, partial control of BA symptoms was observed for 1.5 years: episodes of bronchial obstruction, cough occurred during the period of frequent acute respiratory viral infections, and in the spring. However, since the age of five, episodes of bronchial obstruction had become more frequent, occurring during daytime and night hours under the action of specific (animals, dusty premises, pollen allergens) and non-specific triggers (physical exertion, acute respiratory viral infections). An increase in basic therapy was recommended: ICS doses ranged from medium to high (budesonide 500–1000 μg/day). Due to severe BA exacerbations, the child was repeatedly hospitalized. Taking into account the lack of disease control from the age of six, fixed combinations of LABA with ICS (formoterol + budesonide 4.5/80 μg) at a dose ranging 2–4 inhalations per day were included in therapy, and the course of LTRA (montelukast 5 mg/day) was continued. During the following two years, combined therapy was used to control BA symptoms without severe exacerbations.

At the age of eight, the child's condition worsened. Due to a severe exacerbation of BA, the child was admitted to a hospital, where infusion therapy was performed along with the use of systemic corticosteroids and bronchodilators. During the last hospitalization, the child complained of almost daily episodes of bronchial obstruction, nocturnal symptoms (cough, shortness of breath, distant wheezing). The assessment of BA symptom control based on the results of the ACQ-5 (Asthma Control Questionnaire) was 4 points (uncontrolled BA). The girl continued to receive formoterol + budesonide 4.5/80 μg in therapy, two inhalations twice a day with periods of increasing the dose of ICS (up to 600 μg/day) due to the additional administration of budesonide, montelukast 5 mg/day.

Objective examination during the BA exacerbation

The general appearance was severe. Nasal breathing was very difficult. The respiratory rate was 28–32 per minute. Oxygen saturation was 89%. The chest was of the usual shape. The skin was dry with foci of hypopigmentation in the elbow folds area and the presence of desquamation around the lips. The chest was swollen. The auxiliary muscles were involved in the act of breathing. Percussion sound was vesicular resonance with a boxy tinge. Auscultation: harsh breathing was heard in all departments, wheezing. Blood pressure — 105/80 mmHg, heart rate — 98/min. Height — 142 cm, body weight — 39 kg.

During a comprehensive examination, congenital pathology and hereditary respiratory diseases, immunodeficiency conditions that might occur with the phenomena of bronchial obstruction were excluded. According to the results of an allergological examination (skin test and determination of specific IgE by ImmunoCAP), high sensitization to household allergens (house dust, dust mites), pollen allergens (tree pollen: birch; weeds: wormwood), epidermal (cat) allergens was confirmed. According to a pulmonary function test performed on a JAEGER APS pro device (Germany), restrictive changes were not detected (vital capacity/VC — 92%), but bronchial obstructions were detected (forced expiratory volume in 1 sec/FEV1 — 76%; peak expiratory flow rate at the level of the medium bronchi (PEFR 50) — 48%; peak expiratory flow rate at the level of the small bronchi (PEFR 75) — 34%), the bronchodilator test (salbutamol) was positive (FEV1+20%).

Thus, based on the clinical picture, the dynamics of the disease, clinical laboratory and instrumental diagnostic tests, the child was diagnosed with severe uncontrolled allergic bronchial asthma, I-II stage of respiratory failure, seasonal allergic rhinitis, seasonal allergic conjunctivitis, pollinosis, limited mild atopic dermatitis.

Disease dynamics on the therapy

In order to relieve bronchial obstruction, the child underwent infusion therapy (saline solution, euphyllin up to 12 mg/kg/day, prednisone 2 mg/kg/day) for three days, inhalation therapy through a nebulizer (budesonide 1000 μg/day, salbutamol 8 mg/day). On the therapy, the phenomena of BA exacerbation were stopped. Further, the child was prescribed a combination therapy with LABA/ICS (formoterol + budesonide 4.5/80 μg) two doses twice a day with additional administration of ICS (budesonide 200 μg), montelukast 5 mg/day.

In January 2020, due to the BA severity and insufficient control over the symptoms of the disease, it was decided to initiate GEBD therapy. Taking into account the atopic phenotype of BA (family and personal history of atopic diseases; bronchial obstruction to causally significant allergens from an early age) and the identified BA biomarkers (total IgE 345 IU/mL, polysensitization), GEBD omalizumab became the drug of choice. The dose of the drug was calculated based on the patient's weight and the total IgE level — 300 mg (150 mg in both hands) subcutaneously once every four weeks. On the combined therapy, following 16 weeks, control over BA symptoms was achieved: nocturnal symptoms were relieved, physical activity was increased, the ICS dose was reduced (budesonide 200 μg was discontinued), the ICS dose in combination LABA/ICS was reduced to medium doses, LTRA discontinued.

Due to the sufficient control of BA symptoms, omalizumab was discontinued in June 2022. Further, the child continued to receive basic therapy LABA/ICS (formoterol + budesonide 4.5/80 μg) — one dose twice a day in combination with LABA with sufficient control over BA symptoms. During the flowering period of the trees, the

child noted a decrease in the symptoms of allergic rhinoconjunctivitis. According to the ACB-5, the control of BA symptoms has significantly improved (ACQ-5 = 2 points).

However, six months after discontinuation of omalizumab therapy, despite the continuation of LABA/ICS control therapy, the child showed a catadrome after an acute respiratory illness. Bronchial obstruction attacks appeared 1–2 times a week at night, and physical activity decreased significantly. Despite the therapy correction with an increase in the dose of LABA/ICS to four inhalations per day, episodes of coughing and distant wheezing persisted. The ACQ-5 score was 4.5 points. During the BA exacerbation, high eosinophilia in the blood (780 cells/μl) and high eosinophilia in the rhinocytogram (41%) were noted.

At the same time, the child had an AD exacerbation: common skin rashes appeared (hyperemia, excoriation on the face, body, limbs, severe pruritus, affecting the child's sleep and quality of life). TCS was treated with antihistamines without a lasting positive effect.

Due to the severe course and insufficient control over BA symptoms and the concomitant severe course of AD, it was decided to re-initiate biotherapy. Taking into account the clinical picture of the disease with concomitant AD and uncontrolled BA, laboratory test data (high eosinophilia), it was decided to initiate a targeted therapy with switching of GEBD to dupilumab. The choice of this drug was justified by the severe AD and evidence-based medical data on the positive effect of dupilumab in patients with AD. The drug was administered in an age-appropriate dosage: an initial dose of 400 mg subcutaneously, followed by 200 mg once every two weeks. After 16 weeks of therapy, control over BA symptoms was achieved, with an ACQ-5 of 1.5 points. The girl started attending sports aerobics classes, showing a high exercise tolerance. In February 2024, given the good control over the BA symptoms, the basic therapy was reduced: the child was switched to low doses of LABA/ICS (formoterol + budesonide 4.5/80 μg).

On the dupilumab therapy, a marked relieve of AD was noted after four weeks: there was no exacerbation of the skin condition and pruritus. After 16 weeks, complete relief of the skin manifestations of AD was achieved.

Currently, in the setting of dupilumab therapy, the patient has a positive trend in the absence of AD symptoms and maintains control over the BA symptoms. The disease prognosis is favorable. Taking into account the high sensitization to birch allergens, allergen-specific immunotherapy (AIT) is planned.

CLINICAL CASE DISCUSSION

To date, the issue of selecting an optimal GEBD has not lost its relevance. The emergence of new biopharmaceuticals and an increase in their availability in practical healthcare raises the importance of criteria for the prognostic effectiveness of GEBD in patients. In this regard, the determination of the phenotypic features of the disease and the inflammatory phenotype of BA would be an optimal method for selecting patients with the most complete potential response to a particular type [1, 2].

Currently, it is recommended to determine biomarkers before prescribing biotherapy to predict the clinical response, such as the level of FeNO, the number of eosinophils in the blood and, if possible, in sputum, as well as allergen-specific IgE[5] [14, 16, 17]. It is also necessary to analyze the clinical and anamnestic data, such as the frequency of exacerbations and concomitant diseases, the volume and effectiveness of inhalation therapy, adherence to the use of basic BA therapy, and triggers of asthma exacerbation. However, due to the heterogeneity of the pathogenetic mechanisms of T2 inflammation, the choice of an effective drug may be difficult, especially in pediatric practice. Thus, according to [18], up to one third of patients with severe BA have overlapping criteria for prescribing four GEBD (mepolizumab, benralizumab, dupilumab, and omalizumab), and 75% of patients meet the requirements for prescribing two or more biologics. The study [19] showed that among patients (n = 101) suitable for treatment with mepolizumab, 27–37% also meet the criteria for prescribing omalizumab. It is important to note that not all patients have the same phenotype throughout their lives. Thus, the research study [20] on the temporal stability of AD phenotypes in adults (n = 3320) after 10 years of follow-up found that the initial phenotype was preserved in 54–88% of the study participants. The phenotype can be influenced by environmental factors, allergens, environmental factors, respiratory infection, and ICS therapy [20]. The choice of GEBD also depends on the presence of concomitant pathologies, such as AD, especially severe, since dupilumab is the drug of choice in pediatrics in this group of patients.

In turn, the wrong choice of a target for therapy, and, therefore, the starting monoclonal antibody, frequently leads to a replacement of the targeted drug and an exacerbation of the allergic disease. A retrospective cohort study using data from patients (n = 3531) with severe BA from 11 countries established that 10.8% of patients needed to switch to another GP, and 10.2% stopped treatment due to inefficiency or the development of adverse events [21].

Our patient had a clinically significant sensitization with a confirmed association between allergen exposure and the development of BA exacerbations, which led to a positive response to omalizumab therapy. However, shortly after discontinuation of biotherapy, insufficient control over BA symptoms and severe exacerbation of AD were noted, which was an indication for initiation of therapy with dupilumab. The change of the GEBD contributed to the positive dynamics during both the BA and the AD.

Thus, the described GEBD switching in a patient with severe BA was necessitated by the specific features of the disease course and exacerbation of severe AD.

CONCLUSION

GEBD are the therapy of choice in patients with uncontrolled BA; at the same time, their effect on the pathogenetic mechanisms of the disease differs. The above

[5] Bronchial asthma. Clinical practice guideline. Ministry of Health of Russia; 2024.

clinical case demonstrates the need for a personalized approach when prescribing this type of therapy, taking into account the clinical course of the disease and concomitant pathology in each individual patient.

At present, when deciding on the treatment strategy, as well as when switching between different GEBD, biomarker analysis is used as a basis, including the eosinophil count in peripheral blood and sputum, FeNO measurement, and serum IgE assessment. These biomarkers provide insight into the mechanisms of pathogenesis, allowing the therapy effectiveness to be monitored and the response to treatment to be predicted. However, it should be borne in mind that in patients with BA, the appearance/exacerbation of concomitant pathology (AD, nasal polyposis) may be an important reason for switching to a more effective GEBD.

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