A clinical case of atopic dermatitis with a rapid positive effect from the use of a genetically engineered biological drug in a teenager

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Annotation

Introduction. The instructions for the drug dupilumab indicate that the administration of a single loading dose on the first day leads to the rapid achievement of clinically effective concentrations within 2 weeks, which we saw in the example of our patient and her real clinical response to the first injection.

Presentation of a clinical case. Under our medical supervision was a 17-year-old patient with severe atopic dermatitis, resistant to traditional therapy. Heredity for allergic pathology is burdened: the girl's mother suffers from pollen allergy. Initially before the start of therapy: SCORAD — 88 points, EASI — 48.8 points, IGA — 4, blood eosinophils — 11% (1188 cells/ml), total IgE — 1102.0 IU/ml; the content of nitric oxide in exhaled air (FeNO) is 30 ppb. On April 28, 2021, the patient was administered dupilumab at a dose of 600 mg. Assessment of atopic dermatitis control in points upon admission to the hospital 2 weeks after the first administration of dupilumab: on the SCORAD scale — 44.5 points; EASI — 13.8 points; IGA — 2 points, eosinophils — 9% (1070 cells/ml); total IgE — 840 IU/ml; FeNO — 5 ppb.

Conclusion. This clinical observation clearly illustrates the fact that patients with severe atopic dermatitis who don't respond to first-line therapy can achieve positive clinical results after the first use of a recombinant human monoclonal antibody (IgG4).

Keywords: atopic dermatitis, biotherapy, dupilumab.

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Клинический случай атопического дерматита с быстрым положительным эффектом от применения генно-инженерного биологического препарата у подростка

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Аннотация

Введение. В инструкции к препарату дупилумаб указано, что введение однократной нагрузочной дозы в первый день приводит к быстрому достижению клинически эффективных концентраций в течение 2 недель, что мы и увидели на примере нашей пациентки и ее реального клинического ответа на введение уже первой инъекции.

Изложение клинического случая. Под нашим медицинским наблюдением находилась пациентка 17 лет с тяжелым течением атопического дерматита, резистентного к традиционной терапии. Наследственность по аллергической патологии отягощена: мать девочки страдает пыльцевой аллергией. Исходно до начала терапии: SCORAD — 88 баллов, EASI — 48,8 балла, IGA — 4, эозинофилы крови — 11% (1188 кл/мл), общий IgE — 1102,0 МЕ/мл; содержание оксида азота в выдыхаемом воздухе (FeNO) — 30 ppb. 28.04.2021 больной введен дупилумаб в дозе 600 мг. Оценка контроля атопического дерматита в баллах при поступлении в стационар через 2 недели после первого введения дупилумаба: по шкале SCORAD — 44,5 балла; EASI — 13,8 балла; IGA — 2 балла, эозинофилы — 9% (1070 клеток/мл); общий IgE — 840 МЕ/мл; FeNO — 5 ppb.

Заключение. Данное клиническое наблюдение наглядно иллюстрирует тот факт, что пациенты с тяжелой степенью атопического дерматита, не отвечающие положительным эффектом на первые линии терапии, могут достичь положительных клинических результатов уже после первого применения рекомбинантного человеческого моноклонального антитела (IgG4).

Ключевые слова: атопический дерматит, биотерапия, дупилумаб.

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INTRODUCTION

Atopic dermatitis is a multifactorial genetically determined inflammatory skin disease, characterized by itching, chronic recurrent course, age characteristics of localization and morphology of lesions [1]. To date, there is a constant growth of atopic diseases in the world, which earliest from of manifestation is exactly atopic dermatitis that develops against the backdrop of genetic predisposition to atopy [2].

Modern understanding of AtD pathogenesis is based on immunological peculiarities of lymphocytic infiltrate with an admixture of dendritic cells, an increased level of inflammatory mediators in the affected tissues and defects in the skin barrier [3]. It was revealed that the basis of allergic disease is the change in the correlation of subpopulations of T-helper cells in favor of TH2 phenotype [2]. It is T2-inflammation that the basis of a range of diseases, such as bronchial asthma, allergic rhinitis, chronic polypous rhinosinusitis, atopic dermatitis, eosinophilic esophagitis, etc. [4]. Il-4, Il-13 and IL-5 are key cytokines, involved in a cascade of inflammatory responses in T2-inflammation. It is worth noting that a combination of allergic diseases is common in clinical practice: bronchial asthma (BA), allergic rhinitis and AtD [4, 5]. Considering the contribution of the same cytokines to the

development of inflammation in various conditions, it might seem perspective to use one drug for treating various T2-associated diseases in one patient [4, 6].

The appeared information on the pathogenesis of AtD development prompted scientists to search for drugs, inhibiting cytokines, involved in the process of inflammation. Modern immunology is actively studying the role of particular cells and molecules in the pathogenesis of allergic diseases for diagnosing, treating and monitoring the efficiency of therapy [7]. Dupilumab has become the first targeted biological drug to treat AtD. It is a recombinant monoclonal antibody to IL-4 and IL-13 receptor subunit, which suppresses T2-inflammatory response through inhibition of two key cytokines and might be the preferred drug for treating moderate and severe continuously recurrent AtD [8]. Dupilumab is responsible for inhibiting immune disorders, characterized by Th2 phenotype [9, 10]. Clinical trial, conducted for more than 10 years, has confirmed the efficiency and safety of dupilumab for treating AtD [11–13]. A large number of studies demonstrate the efficacy of dupilumab to treat all cases, characterized by Th2-mediated inflammation [4, 14]. In Russia dupilumab is approved for administration in the treatment of patients aged 6 and over for indications "moderate and severe AtD", under the age 12 years — "bronchial asthma", under the age of 18 years — "polypous rhinosinusitis" [15]. The drug is available in the prefilled syringe, containing 200 or 300 mg of dupilumab. Dupilumab is administered and can be stored at room temperature (до 25 °C) within 14 days if necessary; injection can be done by either the patient (in the hip or abdomen area) or the caregiver (in the upper arm) [4, 16].

DESCRIPTION OF THE CLINICAL CASE

A girl (17 years), burdened by heredity for allergic pathology (the girl's mother suffers from pollen allergy), has been afflicted with atopic dermatitis from an early age. Skin syndrome debuted from 6 months in the form of hyperemia in the upper extremities. The pediatrician diagnosed "sweating fever". At the age of 10 months hyperemia occurred in the upper and lower extremities, the allergist diagnosed "atopic dermatitis, food allergy". Treatment was prescribed with methylprednisolone aceponate with a positive effect.

Skin syndrome relapsed up to 5 years in spring and autumn with the improvement in summer while being at sea. She was hospitalized due to developed streptoderma at the age of 3.

In 2013 she contacted a dermatovenerologist at the place of residence with a severe exacerbation. Local therapy was prescribed. A temporary positive effect was observed for 1–2 months.

The disease had wave-like nature, topical glucocorticosteroid (GCS) drugs were used with a short-term positive effect in courses for 5 years.

Since January, 2020 there has been a pronounced deterioration after stress from the words of the patient. In the spring 2020 she was hospitalized to the regional hospital at the place of residence with complaints of flushing of the skin, itching, scratching, lichenization in the upper and lower extremities, back and face; she got intravenous administration of dexamethasone (4 mg), 0,9 % solution of sodium chloride, antihistamines, external therapy with GCS with no positive effect.

Due to refractoriness to the therapy, she has repeatedly received inpatient treatment since March, 2020. There was constant intake of non-sedating antihistamines and topical glucocorticosteroids; systemic antihistamines in the hospital.

Allergy testing (21.04.2020) (S-IgE): pollen (meadow grass — 2 class); household (house dust— 3 class); epidermal (cat hair — 3 class, dog hair — 2 class); food (chicken eggs — 3 class).

There are no cats and dogs in the patient's house, no chicken eggs consumed and regular wet cleaning.

In December, 2020, due to persistent rash, the patient went to the hospital at the new place of residence, where she got therapy with no positive effect. She received standard care in FSBI "State Scientific Centre of Dermatovenereology and Cosmetology", the Ministry of Health of Russia in conditions of 24-hour hospital in December, 2020. In March, 2021 due to the appearance of new rashes, she returned to the FSBI "SSCDC", the Ministry of Health, where with regard to severity and prevalence of the skin patho-

Table 1. **Comparative data of clinical manifestations**
Таблица 1. **Сравнительные данные клинических проявлений**

Date	SCORAD	EASI	IGA
26.04.21	88 points	48,8 points	4 points
11.05.21	44,5 points	13,8 points	2 points

Table 2. **Comparison of laboratory data**
Таблица 2. **Сравнение данных лабораторных показателей**

Date	IgE total	Eosinophils	FeNO
27.04.21	1102,0 IU/ml	11 % (1188 cells/ml)	30 ppb
11.05.21	840 IU/ml	9 % (1070 cells/ml)	5 ppb

logical process Repeated therapy is recommended under the conditions of 24-hour hospital.

Since 24.03.21 she has got immunosuppressive therapy after another hospitalization (100 mg of Cyclosporin 1 capsule twice a day). Given torpidity and severity of the skin pathological process, it is suggested to consider prescribing the patient genetically engineered biological therapy in the case of failure of immunosuppressive therapy.

One month later, 26.04.2021, the patient was hospitalized in Rostov-on-Don for examining and starting genetically engineered biological therapy with dupilumab, regarding ineffective therapy.

The assessment of atopic dermatitis control in points upon admission to the hospital before dupilumab administration: on the SCORAD scale — 88 points; EASI — 48,8 points; IGA — 4 points.

The patient complained about skin rashes in the scalp area, face, neck, torso, upper and lower extremities, accompanied by severe itching, a feeling of tightness and burning of the skin.

Laboratory indicators: blood eosinophils (CBC) for 27.04.2021 — 11 % (1188 cells/microlitre). Total IgE — 1102,0 IU/ml.

27.04.2021: there was the measurement of exhaled nitric oxide (FeNO) — 30 ppb, with the norm from 0 to 19 ppb. And yet, the patient never reported signs of suffocation or coughing fits.

28.04.2021 dupilumab was administered at a dose of 600 mg (initial dose).

In 2 weeks, the patient was hospitalized to administer the second dose of the drug.

The assessment of atopic dermatitis control in points upon admission to the hospital 2 weeks after the administration of the first dose of dupilumab (Table 1): on the SCORAD scale — 44,5 points; EASI — 13,8 points; IGA — 2 points.

Laboratory indicators in 2 weeks (Table 2): eosinophils — 9 % (1070 cells/ml); total IgE — 840 МЕ/мл; FeNO — 5 ppb.

The patient gave consent to receive biological therapy and use the obtained results of the examination for scientific purposes.

Currently, the patient continues biological therapy. Atopic dermatitis is under control.

DISCUSSION

Literature data show that dupilumab, used in adolescents, causes significant improvements of symptoms in the 16th week (randomized placebo-controlled clinical trial (LIBERTY AD ADOL), in which 251 adolescents with severe and moderate atopic dermatitis received 300 mg of dupilumab every 4 weeks) [17]. In our clinical case significant improvement of clinical and laboratory parameters were observed within a week after starting biological therapy, using dupilumab. What allows to verify the drug efficacy and need for further research to produce new effective and convenient treatments of atopic dermatitis. Some studies have data on the early positive effect of dupilumab

application not only in atopic dermatitis, but also in severe bronchial asthma; the effect was noted in the first 2 weeks of the treatment [18].

It has previously been shown that dupilumab both decreases the incidence of new allergy and improves pre-existing allergic conditions [19]. It has also been proven that blocking signaling pathway of IL-4/IL-13 reduces the concentration of many of type 2 inflammatory markers, including IgE, periostin and multiple pro-inflammatory cytokines and chemokines (e.g., eotaxin, TARC) as well as decreases the level of fractional exhaled nitric oxide (FeNO) — the marker of inflammation in the lungs [20]. Due to a decrease in FeNO rate in the clinical case, we can assume that in the future FeNO rates should be evaluated in patients with atopic dermatitis to predict therapy efficiency in the prevention of bronchial asthma.

Biological therapy in its breakthrough action is comparable to antibiotic therapy and vaccination, innovative at the time. Undoubtedly, prospects of biological therapy in allergology are huge and not limited to symptom control. Dupilumab is a successful representative of its class of drugs with a highly favourable profile of efficacy and safety, enabling it to occupy an important niche in therapy of allergic diseases [21].

CONCLUSION

Dupilumab therapy has enabled the patient to achieve a significant improvement during atopic dermatitis:

1. There was clinical improvement on SCORAD, EASI and IGA evaluation index in two or more times;
2. A moderate decline in the level of eosinophils was noted during therapy: initially — 1188 cells/microlitre, in 2weeks — 1070 cells/ml;
3. There was a decrease in the level of total IgE: initially — 1102,0 IU/ml, in 2 weeks — 840 IU/ml;
4. Taking the drug contributed to a reduction in inflammation activity (reduction of FeNO from 30 to 5 ppb);
5. There was improvement in quality of life.

This clinical case makes us think about the prevention of bronchial asthma within the concept of "atopic march" by acting on key targets in immunopathogenesis of T2-associated diseases.

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THE AUTHORS' CONTRIBUTION TO THE WORK

Ella V. Churyukina — curation, treatment of patients, review of literature, collection and analysis of literary sources, writing and editing the article.

Ekaterina A. Portnyaga — curation of patients, diagnostic monitoring of patients, review of literature, collection and analysis of literary sources, preparation and writing of the article.

All authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work.

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