АТОПИЧЕСКИЙ ДЕРМАТИТ ЯВЛЯЕТСЯ ОДНИМ ИЗ НАИБОЛЕЕ РАСПРОСТРАНЁННЫХ ВТОРИЧНЫХ ЗАБОЛЕВАНИЙ У ДЕТЕЙ, РАЗВИТИЕ КОТОРОГО ОБУСЛОВЛЕНО ВОЗДЕЙСТВИЕМ РАЗЛИЧНЫХ ПРОВОЦИРУЮЩИХ ФАКТОРОВ.

Валиев Нумон Азизуллаевич
ассистент кафедры педиатрии № 2
Бухарский государственный медицинский институт

Аннотация: Атопический дерматит представляет собой хроническое воспалительное заболевание кожи, характеризующееся чередованием периодов ремиссии и обострения. Данное заболевание существенно снижает качество жизни больных детей, а также членов их семей. Топические кортикостероиды остаются основой терапии атопического дерматита. Начиная с двухлетнего возраста, в качестве терапии второй линии могут применяться топические ингибиторы кальциневрина. При тяжёлом течении заболевания, резистентном к стандартной терапии, используется циклоспорин А, тогда как системные пероральные глюкокортикостероиды назначаются лишь в исключительных случаях. Биологическая терапия является современным и перспективным направлением лечения и может в будущем заменить иммуносупрессивную и гормональную терапию у пациентов с прогрессирующим течением атопического дерматита.

Ключевые слова: атопический дерматит, тяжёлое течение, дети, лечение, глюкокортикостероиды, циклоспорин А, наружная терапия, антигистаминные препараты, психосоматические расстройства.

ATOPIC DERMATITIS REPRESENTS ONE OF THE MOST COMMON SECONDARY DISEASES IN CHILDREN, INFLUENCED BY VARIOUS PROVOKING FACTORS.

Valiev Nu'mon Azizullaevich
Assistant, Department of Pediatrics No. 2,
Bukhara State Medical Institute

Abstract: Atopic dermatitis is a chronic inflammatory disorder of the skin characterized by alternating phases of remission and exacerbation. The disease significantly impairs the quality of life of affected children as well as their family members. Topical corticosteroids remain the cornerstone of therapy for atopic dermatitis. From the age of two years, topical calcineurin inhibitors may be used as a second-line treatment option. In severe cases that are refractory to conventional therapy, cyclosporin A is administered, while systemic oral glucocorticoids are used only in exceptional circumstances. Biological therapy represents a modern and promising approach and may potentially replace immunosuppressive and hormonal treatments in patients with a progressive course of atopic dermatitis.

Keywords: atopic dermatitis, severe disease course, children, treatment, glucocorticosteroids, cyclosporin A, topical therapy, antihistamines, psychosomatic disorders

Introduction. Atopic dermatitis (AD) continues to be a significant challenge in pediatrics due to its early manifestation, the growing number of therapy-resistant forms, and its high prevalence among pediatric dermatoses [1]. The disease frequently coexists with or precedes the onset of bronchial asthma and pollinosis [2]. Clinical manifestations of AD substantially impair a child's social adaptation and overall quality of life, while its chronic recurrent course leads to increased costs associated with treatment and rehabilitation [3]. Atopic dermatitis is a multifactorial inflammatory skin disorder that arises from the interaction of genetic predisposition with specific environmental factors. Despite advances in medical science, the introduction of novel diagnostic approaches, and progress in molecular allergology, AD remains insufficiently understood, as the mechanisms underlying disease progression have not yet been fully elucidated. The pathogenesis of AD is generally described as two closely interconnected processes: disruption of the skin barrier and the subsequent development of immune-mediated inflammation. These mechanisms account for the characteristic clinical features of AD, including pruritus, edema, erythema, and skin dryness [4]. Impairment of keratinization processes, increased transepidermal water loss, damage to key structural proteins (filaggrin, involucrin, loricrin, claudins), and alterations in lipid composition, particularly ceramides, result in a reduction of the skin's protective function [5]. This barrier dysfunction facilitates the penetration of exogenous substances and microorganisms, initiating a cascade of immunological responses. Consequently, dysregulation of humoral immunity occurs, accompanied by activation of Th2 lymphocytes and enhanced production of cytokines such as IL-4, IL-13, IL-5, IL-31, and IL-10.

Proinflammatory cytokines suppress epidermal differentiation, reduce the synthesis of antimicrobial peptides, and induce keratinocyte hyperplasia and apoptosis, thereby further weakening and disrupting the skin barrier function [6]. These inflammatory mechanisms form a self-perpetuating "vicious cycle" that maintains pathological activity. At present, key causes of impaired skin barrier function, which play a central role in the pathogenesis of atopic dermatitis (AD), have been identified. In addition to pronounced skin dryness associated with increased transepidermal water loss and sweating disturbances, heightened sensitivity of cutaneous receptors to methacholine is observed. Furthermore, the absence of a normal protective hydrolipid film facilitates direct contact between environmental antigens and the stratum corneum. Significant attention is currently focused on filaggrin, a crucial protein involved in epidermal cell differentiation and formation of the skin barrier [7–9]. By aggregating keratin and promoting apoptosis of keratinocytes in the cornified layer, filaggrin limits transepidermal fluid loss. Identification of mutations in the filaggrin gene (FLG) has enabled recognition of one of the genetic markers predisposing individuals to the development of AD [5]. Although various hypotheses exist regarding the initial trigger of inflammation, Th2-mediated inflammation is consistently present, and immune dysregulation in AD is considered systemic in nature [10–12]. Disease onset and exacerbations may occur during stress of various origins, provided that its intensity and duration exceed the adaptive capacity of the body's regulatory systems. Risk factors are conventionally divided into internal (uncontrolled), external (controlled), and conditionally controlled categories. External factors often act as triggers of disease exacerbations, with biological and social factors having the greatest clinical relevance. Biological factors contributing to AD include exoallergens, which comprise non-infectious agents (household, epidermal, pollen, food, industrial) as well as infectious agents (bacterial, fungal, and viral). Based on routes of exposure, allergens may be classified as food-related, airborne, injectable, or contact. Interaction between internal factors, such as hereditary predisposition to allergic reactions, and external factors, including prolonged exposure and excessive antigenic load, leads to sensitization and the development of allergic inflammation. Another pathogenic combination involves reduced hereditary tolerance to psychological stress together with external stressors, resulting in neurogenic inflammation and characteristic skin changes seen in AD [13–15]. Studies have demonstrated a positive correlation between stress levels and serum eosinophil counts and IgE concentrations, as well as a significantly

higher prevalence of anxiety and depressive disorders in patients with AD compared to healthy control subjects [16, 17]. Chronic stress contributes to dysfunction of the hypothalamic–pituitary–adrenal axis, exerts immunosuppressive effects, inhibits cellular immunity, and shifts immune responses toward Th2 dominance [18, 19]. Various combinations of external factors ultimately determine the severity and frequency of AD exacerbations. In recent years, the role of food allergy in the development of atopic dermatitis has been actively discussed. If in early childhood it really plays a key role (approximately 30-40% of children with moderate to severe AD have proven sensitization to food allergens), then in older age, in adolescents, there is no connection between the exacerbation of the disease and the consumption of food even obligate allergens. Unjustified restriction of children's nutrition can lead in these cases to a violation of their quality of life and exacerbation of dermatitis due to the chronic stress that develops in the child. Treatment of children with advanced forms of AD is a complex task. This is due not only to the clinical polymorphism of the disease and the involvement of various organs and systems in the pathological process, but also to the early onset of AD (in the first months of life), when the doctor's choice is limited to a certain number of medications used at this age that can stop the symptoms of the disease, as well as the risk of developing systemic side effects with uncontrolled use of hormonal drugs. anti-inflammatory external medications. AD therapy is based on a specific plan and includes: diet therapy, systemic pharmacotherapy (antihistamines, enterosorbents), external therapy (antiseptic external agents, corticosteroids, nonsteroidal drugs), in rare cases, immunosuppressive therapy (cyclosporin A). After achieving remission of the disease, anti-relapse treatment with membrane stabilizers (ketotifen for children under 6 years of age) is used, cosmetics are constantly applied to the skin to soften the skin. Therapeutic nutrition of children with AD is based on an individual plan based on age, clinical manifestations of allergies, the spectrum of sensitization detected, the nutritional status of the patient and the functional state of the digestive system. The main principle of diet therapy in the period of severe clinical manifestations of the disease is elimination diets. At the same time as elimination measures, an extremely important point is the adequate replacement of eliminated products with natural or specialized ones, since regardless of the period of illness, the diet should meet the child's physiological needs for energy, basic nutrients and micronutrients [20, 21]. In cases where the child is on natural or mixed feeding, breast milk is kept in the maximum volume, and the nursing mother is prescribed a hypoallergenic diet. If there is a lack or absence of breast milk, it is important to choose the right formula. According to current recommendations, in the period of severe clinical manifestations of allergies (acute period of AD, gastrointestinal manifestations – blood and mucus in the stool, abdominal pain, regurgitation) if there is a confirmed allergy to cow's milk proteins, it is advisable to prescribe therapeutic mixtures based on highly hydrolyzed milk protein, which is practically devoid of antigenic properties, or amino acid mixtures [40, 41]. External therapy is the gold standard for treating AD. The search for the causes of acute AAD sometimes delays the appointment of external treatment. Without it, the inflammatory process progresses, the skin is colonized by Staphylococcus aureus strains that have a toxin producing properties, which can lead to various serious consequences. External treatment of chronic skin inflammation is a complex task. Patients are prescribed fluoridated corticosteroids containing drugs with an antibiotic for a short period of time to stop inflammation and reduce the degree of colonization of the affected skin with Staphylococcus. After 10-14 days, treatment is stopped, using further drugs of the middle class of biological activity. In cases of severe disease with severe exacerbations of the disease, systemic therapy with corticosteroids is resorted to. Most often, the question of their appointment arises when the SCORAD index, which characterizes the severity of AD exacerbation, exceeds 60. Treatment with systemic corticosteroids in children and adolescents with severe AD is carried out at a dose not exceeding 1.5 mg per 1 kg of body weight of the child once a day for 3-5 days, by parenteral (intramuscular) administration. In rare cases, systemic corticosteroids are administered orally; usually, the decision to use this method of treatment is made by a council of specialists [22, 23,29]. In such cases, the dose of prednisone is 1 mg / kg /day, which allows you to achieve the maximum anti-inflammatory effect. On the one hand, it is necessary to achieve remission of AD quickly enough, and on the other hand, to eliminate the risk of serious side effects both during treatment and after its termination. The use of antihistamines in the period of acute AD is pathogenetically justified. Over the long period of existence of these medicines on the pharmaceutical market (since the middle of the last century), a rich positive

experience has been accumulated. In practice, first-and second-generation drugs are used. First generation drugs, along with antihistamines, have antiseroton in activity, anabolic effect and are allowed for children starting from the first month of life. Short courses of treatment (up to 14 days) are usually recommended during acute AD [24]. Antihistamines are prescribed to young children, sick adolescents often draw the doctor's attention to the fact that this group of drugs does not help them. This is due to the fact that in the development of pruritus in older children, it is not histaminoliberation of mast cells that takes part, but neurogenic inflammation. The use of anxiolytics in severe cases helps the child avoid sleepless nights and improve the quality of life. External treatment is based on anti-inflammatory drugs containing corticosteroids and external catsineurin inhibitors: pimecrolimus and tacrolimus. External treatment of corticosteroids is carried out in stages, using corticosteroids with high biological activity when the severity of the clinical course of the disease increases in the acute period of the disease, followed by the use of drugs with lower activity when the inflammatory process subsides [25]. The mechanism of action of immunosuppressive drugs is associated with the suppression of calcineurin, a molecule necessary to trigger the transcription of pro – inflammatory cytokine genes. In the USA, Europe, and Russia, topical calcineurin inhibitors are widely used in children's practice; extensive experience in their use has been accumulated abroad. In Russia, pimecrolimus 1% cream is approved for use in children from three months of age (in the USA and Europe - from two years). The cream is used only in the moderate course of AD and only as a second line of therapy when the treatment of corticosteroids is ineffective. Tacrolimus ointment 0.03% has been successfully introduced into the treatment regimen for AD in various countries (it was introduced in Russia in April 2011) and, like CORTICOSTEROIDS, it is used for both moderate and severe cases of the disease, since it has a greater anti-inflammatory effect than pimecrolimus [26]. A 6-week course of treatment in the acute period is recommended, followed by its appointment during remission 2 times a week. Systemic antibacterial therapy is carried out only in cases of complicated course of AD, with infection with St.. aureus. The drugs of choice include macrolide preparations, clarithromycin 250 mg 2 times a day. Usually, the course of treatment is 7-10 days. Plasmapheresis and systemic immunosuppressive therapy are rarely performed and only in patients with severe forms of AD in the absence of a positive effect of traditional therapy. During plasmapheresis , it is recommended to remove 30-40% of the circulating plasma volume per session; 3 sessions are performed, 1 time in 4 days; plasma is replaced with protein solutions [27,37]. Systemic immunosuppressive therapy is carried out with cyclosporine A, which belongs to the group of drugs for which the correct choice of the drug dose is critically important due to the risk of developing severe side effects if the therapeutic dose is exceeded, and the low effectiveness of therapy with an insufficient dose of cyclosporine A. Usually prescribed from 2.5 to 5 mg/kg/day in two doses. The minimum course of treatment is 6 weeks, the maximum is 12 months. The usual course of treatment is 12 weeks. During treatment, the level of creatinine, liver enzymes, and electrolytes is monitored, and blood pressure is measured daily [28-30,39]. Recently, there have been data on conducting phase III clinical trials of the biological therapy drugdupilumab, which has shown its high effectiveness in the treatment of moderate and severe forms of AD in adults. Dupilumab is a biologic drug based on monoclonal antibodies directed against the interleukin-4 alpha subunit receptor (IL-4RA). Through this effect, it blocks Th2-lymphocyte (Th2) production of IL4 and IL-13, which play a key role in the pathogenesis of atopic dermatitis

LITERATURE

1. Saroyan A. S., Silina L. V. [Electronic resource] Clinical and immunological features of atopic dermatitis in children of early age / Kursk State Medical University / / Kursk scientific and practical bulletin "Man and his health". 2011. No. 1. URL www.kursk-vestnik.ru (accessed on 16.02.2017).

2. Revyakina V. A., Filatova T. A. [Electronic resource] From atopic dermatitis to bronchial asthma in children / Revyakina V. A., Filatova T. A. / / Medical scientific and practical Journal "Lechashchy vrach", 2006, No. 1. URL www.lvrach.ru (accessed on 16.02.2017).

3. Мухамедова Ш. Т. и др. Внутрибольничная инфекция у новорожденных детей //Биология и интегративная медицина. – 2021. – №. 3 (50). – С. 75-86.

4. Мухамедова Ш. Т. Особенности динамики цитокинов у новорожденных с синдромом системного воспалительного ответа. – 2020.

5. Мухамедова Ш. Т., Юлдашева Г. Г. Состояние материнского организма-предиктор развития неонатальной дезадаптации новорожденных //Global science. Development and novelty. – 2016. – С. 37-39.

6. Мухамедова Ш., Гайбиева Ш. Диагностическое значение показателей цитокинов при синдроме системного воспалительного ответа у новорожденных //Журнал вестник врача. – 2021. – Т. 1. – №. 2. – С. 67-70.

7. Мухамедова Ш., Мухитдинов Ш. КОМОРБИДНЫЕ СОСТОЯНИИ У ДЕТЕЙ С ГЕЛЬМИНТОЗАМИ //Models and methods in modern science. – 2023. – Т. 2. – №. 9. – С. 9-10.

8. Мухамедова Ш., Мухитдинов Ш. КОМОРБИДНЫЕ СОСТОЯНИИ У ДЕТЕЙ С ГЕЛЬМИНТОЗАМИ //Models and methods in modern science. – 2023. – Т. 2. – №. 9. – С. 9-10.

9. Мухамедова Ш., Бахронова Д. РАННЯЯ ДИАГНОСТИКА И ПРОГНОЗИРОВАНИЕ ТЕЧЕНИЯ ССВО У НОВОРОЖДЕННЫХ С НЕИНФЕКЦИОННЫМИ ПЕРИНАТАЛЬНЫМИ ЗАБОЛЕВАНИЯМИ //Инновационные исследования в современном мире: теория и практика. – 2023. – Т. 2. – №. 20. – С. 117-120.

10. Мухамедова Ш. Т. Особенности динамики цитокинов у новорожденных с синдромом системного воспалительного ответа. – 2020.

11. Mukhamedova S. T. The prognostic significance of cytokines in the diagnosis of pathology of newborns./Shakhnoza T. Mukhamedova, Dilnoza R. Hamraeva, Fazolat A. Karomatova //Journal of Natural Remedies. – 2021. – №. 1 (1). – С. 119.

12. Мухамедова Ш., Гайбиева Ш. Диагностическое значение показателей цитокинов при синдроме системного воспалительного ответа у новорожденных //Журнал вестник врача. – 2021. – Т. 1. – №. 2. – С. 67-70.

13. Мухамедова Ш., Мухитдинов Ш. ПОКАЗАТЕЛИ ГУМОРАЛЬНОГО ИММУНИТЕТА У ДЕТЕЙ С ГЕЛЬМИНТОЗАМИ //Естественные науки в современном мире: теоретические и практические исследования. – 2023. – Т. 2. – №. 8. – С. 8-10.

14. Mukhamedova S. T., Navruzova S. I. INFLUENCE OF THE STATE OF METABOLISM OF THE MATERNAL ORGANISM ON THE FORMATION OF NEPHROPATHIES IN NEWBORNS //British Medical Journal. – 2023. – Т. 3. – №. 3.

15. Tolibovna M. S., Rustamovna A. N. Innovative Approach to the Diagnosis of Renal Circulation in Newborn //Central Asian Journal of Medical and Natural Science. – 2023. – Т. 4. – №. 1. – С. 374-3

16. Ilkhomovna K. D. Morphological Features of Tumor in Different Treatment Options for Patients with Locally Advanced Breast Cancer //International Journal of Innovative Analyses and Emerging Technology. – 2021. – Т. 1. – №. 2. – С. 4-5.

17. Khodzhaeva D. I. Changes in the Vertebral Column and Thoracic Spinecells after Postponement of Mastoectomy //International Journal of Innovative Analyses and Emerging Technology. – 2021. – Т. 1. – №. 4. – С. 109-113.

18. Khodjayeva D. I. MORPHOLOGY OF IDIOPATHIC SCOLIOSIS BASED ON SEGMENT BY SEGMENT ASSESSMENT OF SPINAL COLUMN DEFORMITY //Scientific progress. – 2022. – Т. 3. – №. 1. – С. 208-215.

19. Ilkhomovna K. D. Modern Look of Facial Skin Cancer //BARQARORLIK VA YETAKCHI TADQIQOTLAR ONLAYN ILMIY JURNALI. – 2021. – Т. 1. – №. 1. – С. 85-89.

20. Ходжаева Д. И. Современные возможности ультразвуковой диагностики рака кожи лица //Вопросы науки и образования. – 2021. – №. 25 (150). – С. 21-24.

21. Aslonov S. G. et al. Modern Approaches to Oropharyngeal Cancer Therapy //International Journal of Discoveries and Innovations in Applied Sciences. – 2021. – Т. 1. – №. 3. – С. 38-39.

22. Khodjayeva D. I. MORPHOLOGY OF IDIOPATHIC SCOLIOSIS BASED ON SEGMENT BY SEGMENT ASSESSMENT OF SPINAL COLUMN DEFORMITY //Scientific progress. – 2022. – Т. 3. – №. 1. – С. 208-215.

23. Khodjaeva D. I. Magnetic-resonance imaging in the diagnosis of breast cancer and its metastasis to the spinal column //Scientific progress. – 2021. – Т. 2. – №. 6. – С. 540-547.

24. Ilkhomovna K. D. MANIFESTATIONS OF POST-MASTECTOMY SYNDROME, PATHOLOGY OF THE BRACHIAL NEUROVASCULAR BUNDLE IN CLINICAL

MANIFESTATIONS //Innovative Society: Problems, Analysis and Development Prospects. – 2022. – C. 225-229.

25. Khodzhaeva D. I. Modern Possibilities of Ultrasounddiagnostics of Skin Cancer //IJTIMOIY FANLARDA INNOVASIYA ONLAYN ILMIY JURNALI. – 2021. – T. 1. – №. 1. – C. 101-104.

26. Ilkhomovna K. D. Modern Look of Facial Skin Cancer //BARQARORLIK VA YETAKCHI TADQIQOTLAR ONLAYN ILMIY JURNALI. – 2021. – T. 1. – №. 1. – C. 85-89.

27. Fatullayeva B. O. New Covid-19 Coronavirus Infection in the Practice of a Neonatologist and Pediatrician //AMALIY VA TIBBIYOT FANLARI ILMIY JURNALI. – 2023. – T. 2. – №. 10. – C. 227-235.

28. Fatullayeva B. O. FEATURES OF THE COURSE OF PREGNANCY AND CHILDBIRTH WITH COVID-19 INFECTION //BOSHQARUV VA ETIKA QOIDALARI ONLAYN ILMIY JURNALI. – 2023. – T. 3. – №. 10. – C. 39-47.

29. Qurbanov M.K. Clinical features and assessment of laboratory and instrumental indicators of acute suppurative otitis media developed against the background of type 1 diabetes mellitus. A New Day in Medicine. Bukhara, 2025; No. 1 (75): 513–516. (14.00.00; No. 22)

30. Nurov U.I., Qurbanov M.K. Assessment of the immune system status and immunological changes in acute suppurative otitis media. Eurasian Journal of Otorhinolaryngology – Head and Neck Surgery. Bukhara, 2024; No. 3 (3): 51–55. (Letter of the Presidium of the Higher Attestation Commission dated April 6, 2024, No. 353/6)