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Severe Atopic Dermatitis and its Difficult Clinical Management

By Amanda Heloise Lacoski Santos, Sintia Gontijo de Oliveira, Mariana Amorim Barbosa, Amanda Pessoa Coimbra de Melo, Fernando Antonio Marçal, Ysla Vitória Damasceno Dias, Eduardo Fernandes Rodrigues, Vanessa Siqueira Batista de Oliveira, João Vitor Rocha Alves, Júlia Monte Teixeira Magnus, Maria de Fátima da Silva, Debora Alves Silva, Rayssa Blenda Martins, Letícia Maria Dias Nobrega, Pedro Henrique de Lima Nogueira, Philipe Bronzeado Cavalcanti Filho, Laura Resende Kanno, Fernanda Pimpão de Paula, Raphael Vinicius Mendes Abreu & Rodrigo Daniel Zanoni

Abstract- Introduction: This paper will cover new updates on atopic dermatitis as a chronic and inflammatory condition that affects people of all ages but is most common in children. Its etiology involves genetic, immunological, and environmental factors, with risk factors such as maternal exposure during pregnancy, irritants, climate change, pollution, and more.

Methodology: The current study is a literature review, the database of which was taken from the SciELO (Scientific Electronic Library Online) and PubMed platforms.

Results: Atopic dermatitis is a chronic and relapsing disease that affects individuals of all ages, but especially children. It is an inflammatory condition that has a multifactorial etiology involving genetic, immunological, and environmental factors that damage the continuity of the epidermis. The incidence can vary according to geographical region as well as ethnicity. It is generally more common in developed countries, with around 15% to 20% of children and 1 to 3% of adults being affected, and its growth can be explained by urbanization and pollution added to the context, which are significant risk factors for this condition. [1]

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Severe Atopic Dermatitis and its Difficult Clinical Management

Amanda Heloise Lacoski Santos ^α, Sintia Gontijo de Oliveira ^σ, Mariana Amorim Barbosa ^ρ,
Amanda Pessoa Coimbra de Melo ^ω, Fernando Antonio Marçal [¥], Ysla Vitória Damasceno Dias [§],
Eduardo Fernandes Rodrigues ^ν, Vanessa Siqueira Batista de Oliveira ^θ, João Vitor Rocha Alves ^ζ,
Júlia Monte Teixeira Magnus [£], Maria de Fátima da Silva [€], Debora Alves Silva ^ƒ, Rayssa Blenda Martins ^²,
Letícia Maria Dias Nobrega ^ϕ, Pedro Henrique de Lima Nogueira [^], Philippe Bronzeado Cavalcanti Filho ^ᵈ
Laura Resende Kanno ^ᵐ, Fernanda Pimpão de Paula ^ᶜ, Raphael Vinicius Mendes Abreu ^ᶑ & Rodrigo Daniel Zanoni ^ˣ

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Conclusion: In summary, atopic dermatitis is a complex, multifactorial condition that affects individuals of all ages. A clinical diagnosis is essential, and treatment varies according to severity. Recent advances, such as systemic therapies and immunobiologicals, offer new hope for patients with severe forms of the disease.

I. INTRODUCTION

This paper will cover new updates on atopic dermatitis as a chronic and inflammatory condition that affects people of all ages but is most common in children. Its etiology involves genetic, immunological, and environmental factors, with risk factors such as maternal exposure during pregnancy, irritants, climate change, pollution, and more. Genetics plays an important role, and recent studies have identified links with specific chromosomes. The diagnosis is clinical and based on symptoms such as itching and skin lesions characterized by areas of lichenification, papules, and nodules. Differential diagnosis includes other skin conditions and is often associated with other atopic diseases. The treatment of atopic dermatitis varies according to its severity. Moisturizers play a key role, and phototherapy, which uses UV radiation, is an effective option. Topical therapy with corticosteroids and

calcineurin inhibitors is necessary. In more severe and resistant cases, systemic therapies, such as immunosuppressants and immunobiologicals, can be considered. Advances in research and treatment have improved the quality of life of patients with atopic dermatitis, and the approach is multidisciplinary, involving different health professionals. It is essential to understand the treatment options available and adapt them to the needs of each patient.

II. METHODOLOGY

The current study is a literature review, the database of which was taken from the SciELO (Scientific Electronic Library Online) and PubMed platforms. The research was carried out in October 2023, meeting the inclusion criteria of articles from 2017 to 2023 in Portuguese and English, online texts and full texts, theses, master's dissertations, book chapters, monographs, and literature in magazines and scientific journals. Health descriptors (DeCS) were used to better evaluate the texts: "atopic dermatitis", "treatment," and "skin diseases".

III. RESULTS

Atopic dermatitis is a chronic and relapsing disease that affects individuals of all ages, but especially children. It is an inflammatory condition that has a multifactorial etiology involving genetic, immunological, and environmental factors that damage the continuity of the epidermis. The incidence can vary according to geographical region as well as ethnicity. It is generally more common in developed countries, with around 15% to 20% of children and 1 to 3% of adults being affected, and its growth can be explained by urbanization and pollution added to the context, which are significant risk factors for this condition. [1]

Among the risk factors, there are those related to the environment and those related to the individual. As environmental factors, it is possible to list maternal exposure during pregnancy: irritants and agents that cause itching, climate change, humidity, radiation, pollutants, exposure to smoke, very concentrated water, diet, among other factors. Genetics has been gaining

more and more strength in the cause of AD. Recent studies have found that atopic dermatitis is related to chromosome 3p and also to segments 3q14, 13q14, 15q14, and 17q21. In addition, other studies have described the immunological theory that it is explained by the Th2 response, which involves the activation of interleukins and their receptors as well as the activation of some skin barrier genes, such as the LAMA3, TEM 79, FLG2, and LELP1 genes. Atopic dermatitis develops due to a dysfunction in the barrier, an immune alteration that leads to an inflammatory response, or a combination of the two. [1] The diagnosis of atopic dermatitis can be made by the skin's immune system.

The diagnosis of atopic dermatitis is clinical, with pruritus being an obligatory symptom. In addition, the signs and symptoms must be associated with the patient's personal history. The skin lesions are usually characterized by areas of lichenification, papules, and nodules, as well as nummular eczema. Other manifestations include inflammation of the dry lips, infranasal erosion, intra-auricular tears, retroauricular intertrigo, eczema on the fingers, nipple, and pityriasis alba. The presence of erythema varies according to race, with blacks showing gray and Caucasians red. [1,2]

The differential diagnosis includes other skin diseases, such as infections (e.g., scabies), other forms of eczema (allergic contact dermatitis, irritant-toxic eczema, seborrheic eczema), and, in babies, seborrheic dermatitis. Patients often have associated diseases, including other atopic conditions (asthma, allergic rhinoconjunctivitis), rarely vernal keratoconjunctivitis, giant papillary conjunctivitis, superficial punctate keratitis, atopic keratoconjunctivitis, or otitis externa and media. Food allergies are demonstrable in 30% of children with severe atopic dermatitis, and immediate type 1 hypersensitivity to cow's milk, chicken eggs, peanuts, soy, and nuts is common. If atopic dermatitis is suspected, potential psychosomatic, allergic, or environmental triggers should be identified. The importance of these triggers varies greatly between individuals, and their prevention is a component of the personalized treatment plan. The role of dietary factors is often overestimated, particularly in childhood; instead, acute and chronic skin irritations and cold temperatures should always be considered as potential triggers of skin barrier dysfunction. Infections and vaccines can also aggravate atopic dermatitis, but children and adults with atopic dermatitis should be vaccinated. [2]

To help with diagnosis, allergy testing can be useful. The presence of sensitivity to a certain type of food does not imply the need for abstinence or treatment; only clinically relevant food allergies of the immediate type or very marked reactions of the late type are an indication for targeted elimination of the allergen. In cases of doubt, provocative tests should

be carried out under appropriate medical supervision. In cases of persistent atopic dermatitis and hypersensitivity to house dust mite allergens, hypoallergenic mattress covers and frequent washing of pillows and comforters are recommended. What to do in cases of sensitization to pet allergens must be decided individually. Patch testing with contact allergens is recommended for the additional demonstration of allergic contact dermatitis, which is difficult to distinguish from concomitant atopic dermatitis on clinical grounds alone. [3,4,5] In the case of allergic contact dermatitis, it is also possible to test for the presence of allergic contact dermatitis.

In addition to allergic tests, we can analyze eosinophilia. The presence of eosinophilia and elevated serum IgE levels is common in patients with atopic dermatitis (AD), but they are not specific to the condition. Eosinophilia is related to the severity of the disease and the deposition of extracellular proteins in the skin. Elevated serum IgE levels have limited diagnostic value, as high values can suggest allergic sensitization, but normal values do not rule out allergy. Patients with mutations in the filaggrin gene tend to have higher levels of serum IgE. However, IgE dosage is not useful as a biomarker for assessing AD exacerbations, and IgE depletion does not reduce AD symptoms. High levels of IgE in umbilical cord blood may indicate a risk of developing AD at 6 months of age [4].

Atopic dermatitis varies in its presentation, from mild to severe forms that require intensive treatment. To standardize treatment and follow-up, a score called SCORAD has been developed, which takes into account the extent of the disease, the severity of the lesions, and subjective symptoms such as itching. The resulting score classifies AD as mild, moderate, or severe. SCORAD can be calculated quickly and even has apps to make it easier to use. Another score, the EASI, excludes subjective symptoms, allowing for a more objective assessment of lesions in different areas of the body. Both the SCORAD and the EASI are considered the best instruments for assessing the clinical signs of AD, while other instruments have not been recommended due to inadequate measurement properties. [4,5] The EASI is also considered the best instrument for assessing the clinical signs of AD.

Severe atopic dermatitis is characterized by extensive, generalized, red rashes with some degree of inflammation that may have crusts, exudates, and areas of lichenification associated with intense pruritus that interfere with quality of life. In this type of AD, skin infections are more frequent. [4,6] The treatment of atopic dermatitis is not recommended.

Treatment for severe atopic dermatitis is complex, as it often does not respond to conventional therapy. Considering the chronicity of AD and the different levels of severity, the goals of AD treatment are to reduce the extent and severity of lesions; reduce

pruritus and improve sleep quality; maintain normal daily activities; improve quality of life; maximize disease-free periods; prevent infectious complications; and avoid or minimize adverse treatment events.

Improving the skin barrier in atopic dermatitis involves the regular use of moisturizers, which help restore moisture to the skin and reduce dryness, itching, and inflammation. Clinical studies have shown that the use of moisturizers improves the severity of the disease and reduces the need for topical anti-inflammatory medications. The recommended amount varies with age.

Moisturizers for atopic dermatitis contain emollients, occlusive substances, and humectants to maintain hydration, reduce water evaporation, and increase hydration of the stratum corneum. It's important to choose a moisturizer with few ingredients, without fragrances or sensitizers, to avoid allergic reactions. The choice of texture (lotion, cream, or baume) can vary according to preference and climate. It is recommended to apply the moisturizer two or three times a day, especially after bathing and on areas with or without lesions. Daily baths with warm water and physiological pH soaps or bath oils are recommended to avoid drying out the skin. New moisturizers contain ingredients such as cannabinoids, bioactive lipids, and modulators of the microbiome to provide additional benefits to the skin, such as regulating lipid production, reducing itching, and modulating the skin's microbiota. [2,5,6] Phototherapy is a modality used to treat skin lesions.

Phototherapy is a treatment modality for various inflammatory and immune-mediated diseases that uses ultraviolet (UV) wave spectra to irradiate the patient's skin. In atopic dermatitis (AD), two effective modalities are UVA-1 and narrowband UVB (UVB-FE), the latter being safer. Phototherapy acts by suppressing the skin's immune system, reducing the response of lymphocytes involved in AD, improving the skin barrier, and reducing *Staphylococcus aureus* infections. [3,5,6] It is recommended as an adjuvant treatment for atopic dermatitis.

It is recommended as an adjuvant treatment in cases where topical treatments fail before systemic immunosuppressive medications. Efficacy varies between patients, but RUVB-FE has shown benefits in improving eczema and reducing pruritus in clinical studies. The safety and efficacy of phototherapy with RUVB-FE have been proven in patients aged three and over, with remission rates of more than 50% in one year of treatment, especially in children with higher phototypes. However, equipment availability and costs can be limitations to accessing this treatment, and exposure to phototherapy can raise concerns about the risk of skin cancer, especially in pediatric patients. Although it is an effective option, phototherapy faces challenges related to cost, accessibility to equipment,

and possible exposure to skin cancer, especially in children, limiting its use in some regions. New technologies and more affordable devices could improve the availability of phototherapy in the future. [5]

Topical therapy is necessary for all patients, regardless of the severity of AD. This includes the use of topical corticosteroids and topical calcineurin inhibitors as a base treatment. New topical therapies, such as topical phosphodiesterase-4 inhibitors and topical Janus kinase inhibitors, are also emerging, although they are not yet available in Brazil [5, 6, 7].

Topical corticosteroids have a mechanism of action that includes anti-inflammatory, anti-proliferative, and immunosuppressive effects. They are the first treatment option for acute attacks of AD, as long as they are applied correctly, in the appropriate potency for each area, and in the necessary quantity. The potency of the corticosteroid should be adapted to the severity of the lesion and the region treated, avoiding potent corticosteroids in thin-skinned areas, such as the face, and giving preference to medium- and low-potency corticosteroids in children. [6,7] The use of corticosteroids in children is also recommended.

Various approaches can be used for systemic treatment. In cases of recurrent skin infections, especially with *S. aureus*, topical antibiotics can be used. Systemic antibiotics, such as first-generation cephalosporins, may be indicated for extensive surfaces. Immunosuppressants, such as systemic corticosteroids, cyclosporine A (CsA), methotrexate (MTX), azathioprine (AZA), and mycophenolate mofetil (MFM), are reserved for severe and refractory cases. The use of systemic corticosteroids should be extremely cautious due to their side effects. Cyclosporine A (CsA) is recommended as a first-line treatment for severe cases of AD in adults, children, and adolescents. Methotrexate (MTX) is an accessible and low-cost alternative, especially for severe cases. Azathioprine (AZA) is considered a second-line option when cyclosporine is not effective or is contraindicated. Mycophenolate mofetil (MFM) is a third-line therapy used in severe cases, although there is less evidence of efficacy on a large scale. [6] Immunobiology represents a class of drugs that are accessible and affordable, especially for severe cases.

Immunobiology represents a class of pharmacological agents used to treat inflammatory and allergic diseases. They are designed to target mediators of allergic inflammation, such as cytokines, and have played an important role in the treatment of immune-mediated diseases. Currently, these drugs are used to modulate the immune response, including blocking IgE and various cytokines, such as IL-4, IL-13, IL-22, IL-32, IL-17, and IL-23, which play a key role in the pathogenesis of diseases such as atopic dermatitis. Immunobiologicals are considered safe and can be prescribed on the basis of clinical assessment without

the need for extensive laboratory tests, making them a valuable option for patients with moderate to severe atopic dermatitis who do not respond adequately to other treatments. [7] The use of immunobiologicals in the treatment of atopic dermatitis is also important.

Learning about atopic dermatitis and how to treat it properly is important for making sure the patient has a good quality of life. In the worst cases, treating the condition can be more difficult and require the work of many professionals and areas of the patient's life. Studies on new technologies and approaches are increasingly being invested in research, and each year the treatment becomes more effective and evolves for individuals. [1,3]

IV. CONCLUSION

In summary, atopic dermatitis is a complex, multifactorial condition that affects individuals of all ages. A clinical diagnosis is essential, and treatment varies according to severity. Recent advances, such as systemic therapies and immunobiologicals, offer new hope for patients with severe forms of the disease. The multidisciplinary approach and constant research contribute to improving the quality of life of those affected, highlighting the importance of personalized treatment that adapts to individual needs.

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