INTERNATIONAL JOURNAL
of PEDIATRIC DERMATOLOGY

Vol 1. Iss. 2 (July-December, 2024)

Case Report

Hydrotherapy as adjunctive therapy of severe pediatric atopic dermatitis treated with dupilumab

A. M. Mósca-Cerqueira[3], C. Pereira Silva[1], I. C. Soligo Kanaan[3], A. J. P. Faria-Jr[1 2]

[1]Universidade Fundação Oswaldo Aranha, Rio de Janeiro, Brazil
[2]Universidade Federal Fluminense, Niterói, Brazil
[3]Hospital Municipal Jesus, Rio de Janeiro, Brazil

KEYWORDS

atopic dermatitis, dupilumab, hydrotherapy, pediatrics, dermatology

ABSTRACT

Atopic dermatitis (AD) is a chronic inflammatory skin disease with significant morbidity. This report presents the case of a 15-year-old male with severe AD, unresponsive to standard treatments, who showed marked improvement with dupilumab and adjunctive hydrotherapy using Minéraux Beauty Thermal Water™. Over five years of treatment, the patient experienced multiple infections and hospitalizations, with only limited improvement until the introduction of dupilumab and hydrotherapy. The combination therapy resulted in significant lesion resolution and enhanced skin hydration. This case underscores the efficacy of dupilumab as a cornerstone treatment for severe AD and highlights the potential benefits of hydrotherapy as a safe, cost-effective adjunctive therapy. Further research is warranted to explore the synergistic effects of combining immunobiological agents with hydrotherapy in managing severe AD.

CORRESPONDING AUTHOR

Aydamari João Pereira Faria-Jr
VPS, ICHS - Universidade Federal Fluminense
Rua Desembargador Ellis Hermydio Figueira, 783
Bloco A, Sala 212-A
Aterrado, Volta Redonda
RJ - Brazil

aydamari@gmail.com

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1. Introduction

Atopic dermatitis (AD) is a chronic relapsing inflammatory skin disease and is one of the most common illnesses in children. Its prevalence varies by ethnicity and age group, being approximately 17.6% in Italy, 18.6% in Spain and 20.1% in Brazil (1).

The pathophysiology of AD is not yet fully understood, but it appears to be related to a pathological IgE-mediated Th-2 biased immune response. Several factors seem to play a role in its development, including genetic and environmental factors, as well as altered immune responses, which either directly or indirectly modify the skin barrier, alter its microbiome and lead to the characteristic pruritic lesions (2, 3).

Over 20 genetic variations have been linked to AD, many of which involve the epidermal differentiation complex (EDC). The filaggrin (FLG) gene, a member of this complex, is particularly notable, with loss-of-function mutations being extensively studied in relation to AD (2, 4). Experimental and clinical evidence suggest that these genetic variations, either directly or indirectly, reduce skin hydration, contribute to more pronounced transepidermal water loss (TEWL) and hinder local immune responses. These factors are correlated with the severity of AD lesions and predispose the skin to microbial colonization (5, 6).

Multiple environmental factors may contribute to the pathophysiology of AD. Exposure to air pollution, microorganism colonization, aeroallergens, climate, food allergens and water composition ("hard water") seem to play roles in the pathogenesis of AD (2, 7). Moreover, although not completely understood, interactions between genetic and environmental factors may epigenetically modulate AD physiopathology (8).

In this report, we present the case of a 15-year-old male with severe atopic dermatitis who has been followed for the past five years and only improved after treatment with dupilumab and adjunctive hydrotherapy. The purposes of this report are to reiterate the efficacy of dupilumab in the treatment of severe atopic dermatitis and to highlight the potential benefits of hydrotherapy as a safe and cost-effective adjunctive therapy.

2. Clinical case

A 15-year-old male patient, diagnosed with asthma and atopic dermatitis at the age of three, was first seen in the dermatology department of Jesus County Hospital when he was 10 years old, in 2019. His initial SCORAD (SCORing Atopic Dermatitis) was 56.3. In addition to AD, he presented with toilet seat dermatitis and was treated with multiple medications, including cotrimoxazole, tacrolimus, fluconazole and loratadine.

At age 11, in 2020, his SCORAD was 56.9, and methotrexate, folic acid and risperidone were prescribed. He experienced multiple skin infections, initially treated with clarithromycin and later with amoxicillin and clavulanate. He was subsequently admitted to the hospital for treatment with oxacillin, vancomycin and fluconazole; methotrexate was discontinued. As he began exhibiting depressive behaviors, he started psychotherapy and psychiatric follow up. He was discharged after 14 days of hospitalization.

In 2021, his SCORAD was 62. He was admitted in the hospital once again due to cellulitis and treated with levofloxacin. After discharge, dupilumab was prescribed, but he could not adhere to the treatment due to local and legal distribution issues.

In 2022, he was hospitalized once more due to a severe infection related to his AD and treated with vancomycin, clindamycin and loratadine. He was on escitalopram, fluoxetine and risperidone for his mental health treatment. In 2023, he was prescribed fluvoxamine but discontinued it after approximately six months due to a possible worsening of his skin lesions.

In June of 2023, the patient initiated regular use of dupilumab. Hydrotherapy, using Minéraux Beauty Thermal Water™, was introduced initially through immersion baths, conducted for at least 20 minutes twice daily over seven days. Subsequently, it was used as a topical adjunctive therapy. Following this combined treatment, the patient's lesions exhibited further improvement.

3. Discussion

A comprehensive review of AD and its treatment is beyond the scope of this paper, but some key aspects must be mentioned. AD, especially in its severe form, poses challenges that extend far beyond skin lesions: it impacts patients' psychological and psychiatric health, as well as in their social lives. It also imposes a financial burden, as AD treatment typically involves multiple remissions, complications and infections, which further add to the economic toll on patients and their families (9, 10).

In general, managing severe AD requires a multifaceted approach, including controlling skin inflammation - either topically, systemically or both -, to the elimination (or mitigation) of environmental triggers. All initiatives aim to repair and restore the skin barrier. Treatment should be viewed as a continuum, with behavioral and pharmacological interventions intertwined to reduce both TEWL and local inflammation (11).

Patients should be advised to identify and avoid trigger factors, keep their skin protected and ensure adequate hydration. Suitable moisturizers and creams can help control skin scaling. Baths should be brief and the water should not be too hot. All household cleaning products, including laundry detergents, should be restricted to neutral, fragrance-free detergents; bleach and fabric softeners should also be avoided (3).

Pharmacological interventions include broad action drugs such as corticosteroids, cyclosporine and methotrexate, which reduce the inflammatory cascade dysregulation characteristic of AD physiopathology. Topical corticosteroids are the first-line treatment for AD and are safe and effective when properly used (12).

More targeted immunomodulatory drugs have recently been added to the AD treatment arsenal. Pimecrolimus and tacrolimus are topical options that inhibit calcineurin, leading to reduced secretion of pro-inflammatory cytokines and cellular recruitment (12, 13). Dupilumab, a monoclonal antibody that selectively inhibits IL-4 and IL-13 via a shared subunit receptor, plays a central role in controlling the characteristic AD Th2 skewed immune response. Dupilumab is regarded as the most effective biological treatment for severe AD and is also considered safe for pediatric patients (14, 15).

Adjunctive therapies have historically been used alongside pharmacological therapies in the management of AD. Hydrotherapy is one of the most commonly practiced adjunctive therapies, either in natural settings (e.g. balneotherapy) or topically (16). Despite controversies and difficulties understanding the mechanisms behind the benefits of hydrotherapy and thermal water (17), there is sufficient evidence supporting its benefits as an adjunctive therapy for AD patients (18, 19).

Hydrotherapy can address both AD skin dehydration and the adverse effects of hard water. Thermal and topic waters with specific mineral compositions can reduce TEWL, maintain skin hydration and alleviate AD symptoms. Replacing traditional hard water with softer water (e.g. with lower calcite and dolomite content) has been shown to improve AD severity (20). The benefits of hydrotherapy may also be attributed to its bacteriostatic properties, to its mineral composition, to its non-pathogenic microbiota or a combination of these (16). Overall, hydrotherapy has minimum side effects, is safe and affordable as an adjunctive therapy for AD.

This report presents the case of a 15-year-old boy with severe and refractory AD, characterized by recurrent infections and multiple hospital admissions. Upon his first visit to the Jesus Hospital Dermatology outpatient clinic, at the age of 10, his SCORAD was higher than 50. Despite various treatment approaches and many hospitalizations, his lesions did not improve until he began using dupilumab, alongside a regimen of thermal water adjunctive treatment.

Figure 1 shows the patient's condition before starting dupilumab, and Figure 2 was taken after six months of dupilumab treatment. The dupilumab-mediated improvement is evident, though some AD hallmarks are still present (e.g. dry scaly skin throughout the trunk and legs). Figure 3 illustrates the patient's skin condition after a 7-day immersion hydrotherapy treatment, where noticeable skin hydration and overall improvement were observed.

Fig. 1. *Intraepidermal vacuolation with keratohyaline granules. H-E 400x.*

Fig. 2. *Skin appearance after six months of dupilumab treatment and before hydrotherapy.*

Fig. 3. *Skin appearance after one week of immersion hydrotherapy with Minéraux Beauty Thermal Water™ following six months of dupilumab treatment.*

It is well known that the most appropriate experimental design to evaluate the efficacy of treatments is double-blind randomized controlled trials (RCTs). Nonetheless, case reports can often provide invaluable insights into new or underestimated treatments. Aside from the efficacy of dupilumab treatment, this report also presents the case of a significant potential skin improvement related to the use of hydrotherapy, represented here by Minéraux Beauty Thermal Water™, observed six months after initiating dupilumab.

The mechanisms by which hydrotherapy improves skin lesions are yet to be fully unveiled, but as previously mentioned, as a soft-water treatment, it may contribute to reducing TEWL and skin dehydration, among other mechanisms that are crucial for promoting or accelerating skin healing processes. The association of an immunobiological agent with immunoregulatory properties, such as dupilumab, with hydrotherapy, as represented by Minéraux Beauty Thermal Water™, may have a synergistic effect in the recovery of skin lesions related to severe atopic dermatitis, and more studies are needed to further address the full potential of this association.

4. Conclusion

This report underscores the efficacy of dupilumab in treating severe AD, which remains underreported in the literature. Additionally, it highlights the potential benefits of hydrotherapy as an adjunctive treatment for severe AD. In summary, this report reinforces dupilumab as a safe and effective option for treating severe AD. It also serves as an important preliminary step in exploring the efficacy of high-quality thermal water, represented here by Minéraux Beauty Thermal Water™, as a favorable cost-benefit adjunctive therapy for severe AD lesions, which should be considered in the treatment repertoire for AD.

FUNDING

No funding was received.

DISCLOSURE

All authors report no conflict of interest.

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