Etanercept therapy for difficult-to-control erythrodermic psoriasis. A case report

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Case Report

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Background: Erythrodermic Psoriasis affects less than 2% of Psoriasis patients and is defined by erythema and hyperkeratosis that affects at least 90% of the total body surface. Due to the extensive skin involvement, patients may present systemic symptoms, making this pathology a risk to life. The case of a 68-year-old female patient with Erythrodermic Psoriasis is presented, who had intolerance to conventional treatments and multiple comorbidities. The patients history reveals a progression of two months with the presence of diffuse erythema, peeling, pruritus, skin ardor, fever, chills and general discomfort. Physical examination reveals erythematous lesions, desquamative with hyperkeratosis that converge with each other, causing pain and intense itching. Skin biopsies confirmed the presumptive diagnosis. IL-6 and IL-8 participate in hyperkeratosis and formation of new vessels; their elevated levels are related to the severity of the pathology. ELISA and RT-qPCR results have shown that Etanercept decreased the production of these cytokines. Following a comprehensive analysis, management with Etanercept was initiated, resulting in significant clinical improvement. The use of these agents should be individualized and tailored to each patient's characteristics.

Psoriasis is a chronic autoimmune disease that affects 1-3% of the global population, characterized by dermal lesions with epidermal hyperplasia, hyperkeratosis, and infiltration of immune cells [1]. There are different phenotypes, one of which is Erythrodermic Psoriasis, a severe and rare variant [2]. Erythrodermic Psoriasis affects less than 2% of Psoriasis patients and is defined by erythema and hyperkeratosis that affects at least 90% of the total body surface. Due to the extensive skin involvement, patients may present systemic symptoms such as pruritus, fever, arthralgia, asthenia, fever, lymphadenopathy, electrolyte imbalance and tachycardia, making this pathology a risk to life [2,3].

Being a systemic immune disease, Psoriasis is associated with a high risk of comorbidities. Recent advancements in biological agents have improved the effectiveness and safety of the management of Erythrodermic Psoriasis. Biological therapies while targeting pro-inflammatory cytokines not only address Psoriasis but also help manage associated comorbidities [4].

There are different mediators involved in the pathogenesis of Psoriasis, including neutrophils, T lymphocytes and pro-inflammatory cytokines such as TNF-α, IL-23, IL-6 and IL-8. Blocking TNF-α activity, as achieved with Etanercept, a soluble recombinant human fusion protein acting as a competitive inhibitor of endogenous TNF, leads to improvement in Erythrodermic Psoriasis progression [1,5].

The case of a patient with Erythrodermic Psoriasis is presented, who had intolerance to conventional treatments and multiple comorbidities. Following a comprehensive analysis, management with Etanercept was initiated, resulting in significant clinical improvement.

Case report

The case of a 68-year-old female patient with a 20-year diagnostic Psoriasis history is presented. She has multiple comorbidities, such as Systemic Arterial Hypertension, Obesity, Primary Hypothyroidism, Obstructive Sleep Apnea Syndrome, Chronic Venous Insufficiency, recurrent Depressive Disorder, Migraine, Heart Failure, Chronic Renal Disease, Prolactinoma and a Pulmonary Nodule. In addition, she suffers from complications related to psoriasis, specifically Psoriatic Arthritis diagnosed within the past year.

The patient's history reveals a progression of two months with the presence of diffuse erythema, peeling, pruritus, skin ardor, fever, chills and general discomfort. Physical examination reveals erythematous lesions, desquamative with hyperkeratosis that converge with each other, causing pain and intense itching, covering approximately 90% of the body surface area, with the face being the only area spared. (Figure 1, 2)

Initial laboratory findings revealed leukocytosis (14,000 c/dL) and elevation of acute phase reactants (VSG 45 mm, PCR 212 mg/L). Due to the extension of dermatological lesions, the diagnosis of Erythrodermic Psoriasis is integrated.

In the last year, the patient received initial management with Methotrexate, however, 3 months later she began with dyspnea, cough and desaturation.

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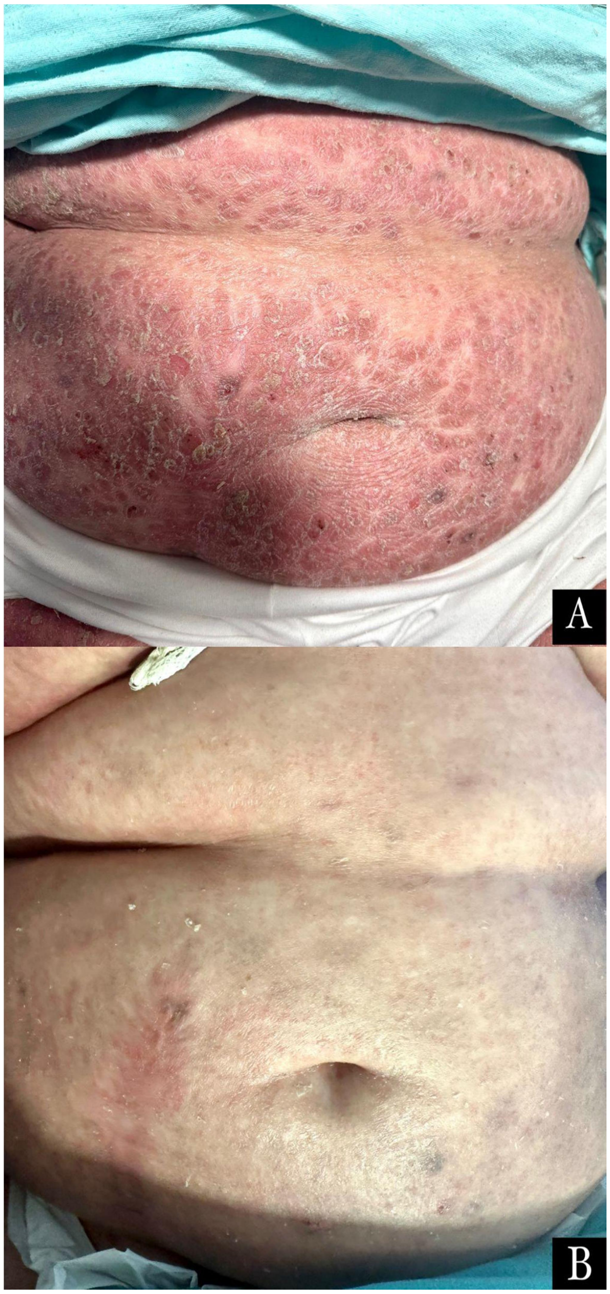

Figure 1. Patient's abdomen upon admission. B.- Abdomen of patient after 2 weekly doses of Etanercept.

Figure 2. Upper limb upon admission B.- Upper limb after 2 weekly doses of Etanercept.

A thorax tomography evidentiated interstitial nonspecific pattern pulmonary disease. Management is stopped under the suspicion of toxicity. Subsequently, after the last valuation by dermatology, the beginning of Cyclosporine is proposed, however, it is contraindicated by nephrology when presenting a 2.2 mg/dl creatinine.

Therefore, our internal medicine service evaluated the patient and determined that the next therapeutic step is to administer an anti-TNF medication. Protocol begins by obtaining skin biopsies confirming the presumptive diagnosis. Cultures yielded negative results, as did serologies for HIV, HBV, and HCV. Additionally, the tuberculin test showed no reaction and biopsy results of the pulmonary nodule ruled out malignancy and tuberculosis. Echocardiogram with 62% LVEF, classified as ACC/AHA C NYHA I. Current GFR 49 ml/min/1.72 m2 according to the latest laboratories.

The case is reviewed in collaboration with the dermatology service and Etanercept therapy is selected as the best option due to its favorable security profile for our patient. After completing the initial assessment, we initiated subcutaneous administration of Etanercept at a dosage of 50 mg once weekly. By the second week of treatment, the patient showed nearly complete resolution of erythema and overall symptoms, without any apparent adverse reaction. Our plan is to continue the Etanercept prescription for 24 weeks and follow-up in ambulatory consultation.

Discussion

Erythrodermic Psoriasis has a significant negative impact on patients' quality of life, even being

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potentially fatal [1]. Conventional treatments, such as topical glucocorticoids, cyclosporine and methotrexate, have shown limited efficacy, often resulting in relapses upon discontinuation. The use of biological agents has represented a significant advance in the resolution of acute episodes, including Etanercept [5].

It has been demonstrated that TNF-α is a main cytokine related to the pathogenesis of Psoriasis, it participates in the regulation of keratinocyte proliferation, immune activation and production of pro-inflammatory cytokines. IL-6 and IL-8 participate in hyperkeratosis and formation of new vessels; their elevated levels are related to the severity of the pathology. ELISA and RT-qPCR results have shown that Etanercept decreased the production of these cytokines [1]. A prospective clinical trial in 2006 demonstrated the effectiveness of Etanercept in treating Erythrodermic Psoriasis. This 24-week trial involved 10 patients. Remarkably, 6 out of the 10 patients achieved PASI75 (greater than 75% decrease in disease activity) by the end of the trial, highlighting the efficacy of Etanercept as a treatment option. Additionally, several case reports have supported the effectiveness of Etanercept [5,6].

There are differences in the impact of biologic agents on comorbidities, so a comprehensive clinical history is important in selecting the appropriate treatment. In relation to cardiovascular events, it has been found that patients with Psoriasis have an elevated risk of cardiovascular mortality. A cardioprotective effect has been found in patients treated with TNF-α inhibitors [4,7], which made it an option to consider in the management of our patient with multiple cardiovascular comorbidities. Another pathology present in our patient and in which the use of biologic agents has been studied is Psoriatic Arthritis, where the treatment of choice is TNF-α inhibitors [8].

There are adverse effects reported in the use of TNF-α inhibitors. These medications have been associated with an elevated risk of infections, including tuberculosis, exacerbation of lupus, and paradoxical reactions [7]. It's important to note that the use of Etanercept in Erythrodermic Psoriasis remains off-label. There is limited information available to guide management, with most data and clinical evidence derived from small case series and individual case reports. The duration of remission and the risk of relapse after discontinuing the drug are poorly understood. There is a need to expand research efforts and evidence regarding Erythrodermic Psoriasis [2-5].

Conclusion

The use of biological agents for the management of Erythrodermic Psoriasis has not been well established. In the case of our patient, given multiple comorbidities and poor tolerance to first-line treatment, we conducted a thorough analysis of the various available options, including biological agents. The use of these agents should be individualized and tailored to each patient's characteristics, with close monitoring. The quality of life of patients with Erythrodermic Psoriasis can improve considerably by choosing the appropriate therapy for them. It is important to publish cases like this to support the research on the use of these therapies.

Conflicts of interests

The authors declare no conflicts of interests.

References

1. Li S, Li G, Li X, Wu F, Li L. Etanercept ameliorates psoriasis progression through regulating high mobility group box 1 pathway. Skin Res Technol. 2023 Apr;29(4):e13329.
2. Potestio L, Camela E, Cacciapuoti S, Fornaro L, Ruggiero A, Martora F, et al. Biologics for the Management of Erythrodermic Psoriasis: An Updated Review. Clin Cosmet Investig Dermatol. 2023 Aug 4;16:2045-2059.
3. Lo Y, Tsai TF. Updates on the Treatment of Erythrodermic Psoriasis. Psoriasis (Auckl). 2021 Jun 9;11:59-73.
4. Jiang Y, Chen Y, Yu Q, Shi Y. Biologic and Small-Molecule Therapies for Moderate-to-Severe Psoriasis: Focus on Psoriasis Comorbidities. BioDrugs. 2023 Jan;37(1):35-55.
5. Shao S, Wang G, Maverakis E, Gudjonsson JE. Targeted Treatment for Erythrodermic Psoriasis: Rationale and Recent Advances. Drugs. 2020 Apr;80(6):525-534.
6. Li X, Jiang M, Chen X, Sun W. Etanercept alleviates psoriasis by reducing the Th17/Treg ratio and promoting M2 polarization of macrophages. Immun Inflamm Dis. 2022 Dec;10(12):e734.
7. Kamata M, Tada Y. Efficacy and Safety of Biologics for Psoriasis and Psoriatic Arthritis and Their Impact on Comorbidities: A Literature Review. Int J Mol Sci. 2020 Mar 1;21(5):1690.
8. Thatiparthi A, Martin A, Liu J, Egeberg A, Wu JJ. Biologic Treatment Algorithms for Moderate-to-Severe Psoriasis with Comorbid Conditions and Special Populations: A Review. Am J Clin Dermatol. 2021 Jul;22(4):425-442.

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