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Allopurinol-Induced Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis Successfully Treated with a Single Dose of Etanercept

Mariele Bevilaqua[1*], Adriana Marcela Serrano Ambrosi[1], Raquel Kupske[1], Marina Gianisella[2] and Rodrigo Pereira Duquia[2]

[1]Department of Dermatology, Irmandade Santa Casa de Misericórdia de Porto Alegre Hospital, Porto Alegre- Rio Grande do Sul, Brazil

[2]Universidade Luterana do Brasil - Canoas, Brazil

[*]**Corresponding author:** Mariele Bevilaqua, Department of Dermatology, Irmandade Santa Casa de Misericórdia de Porto Alegre Hospital, Porto Alegre- Rio Grande do Sul, Brazil, Tel: +55 (51) 996447728; E-mail: dramarielebevilaqua@gmail.com

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Dear Editor,

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are potentially fatal cutaneous adverse reactions usually triggered by medications, allopurinol is frequently associated with this condition, affecting skin and mucous membranes. It typically occurs within days or weeks after the drug's use [1-3]. Scientific evidence suggests that etanercept may be a promising treatment [2].

This case reports a 43-year-old female with skin injuries, which appeared 13 days after starting allopurinol 300 mg/day to treat hyperuricemia. She presented with diffuse erythematous rash, including palms and soles, ulcerated lesions in the oral mucosa, vaginal inner lips, and ocular erythema. Severity-of-illness score of toxic epidermal necrolysis (SCORTEN) was two on the first day of admission.

Approximately 48 hours after the onset of the rash, she progressed with fever and epidermal detachment in the back area (FIG. 1 a-b). A skin biopsy was performed, and histopathological findings were consistent with TEN (FIG. 2 a-b).

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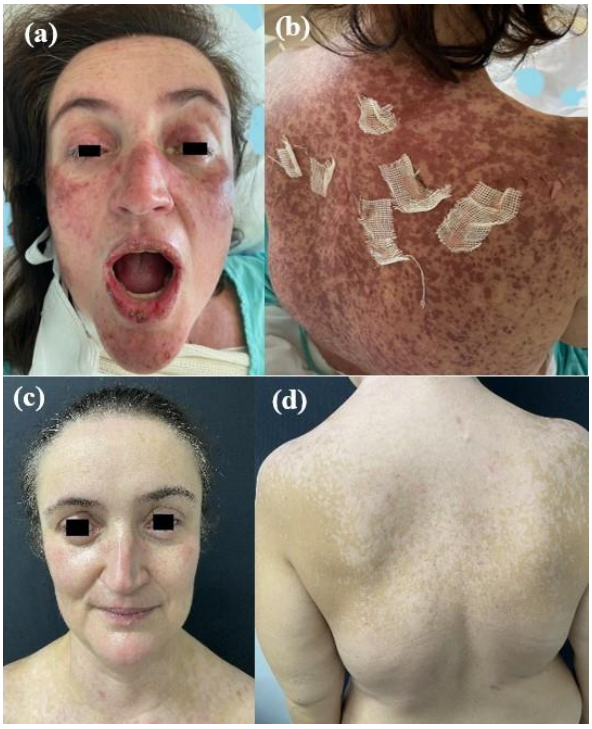

FIG. 1. **(a-b) Mucosal erosions with epidermal detachment. (c-d) The patient one month after a single dose of subcutaneous etanercept 50 mg.**

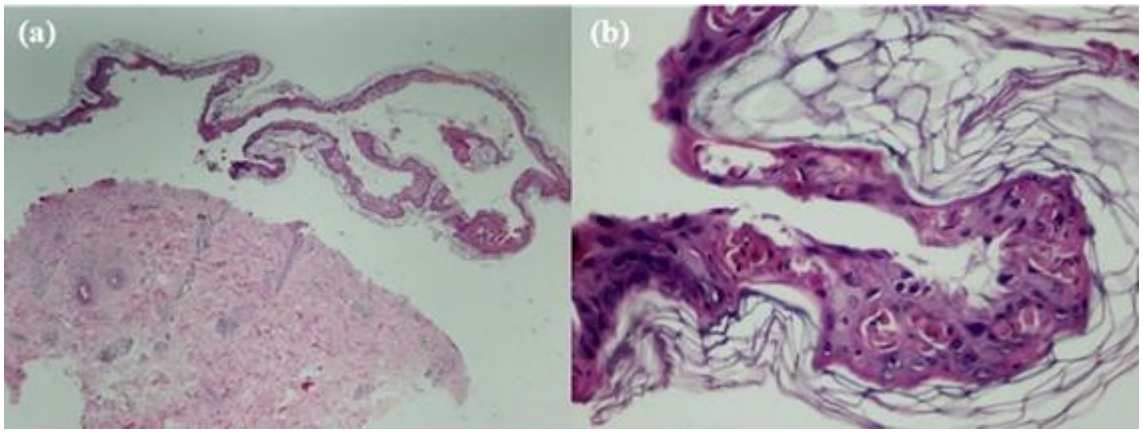

FIG. 2. **(a). Skin histopathology (Hematoxylin and eosin, 40x): Interface dermatitis with vacuolar damage and satellite necrosis of keratinocytes affecting the full thickness of the epidermis, forming subepidermal vesicles. (b). (Hematoxylin and eosin, 100x): Perivascular lymphocytic infiltrate in the upper dermis and close-up of the area of necrotic keratinocytes.**

Initial treatment consisted in intravenous methylprednisolone, corresponding to 1 mg/kg/day of prednisone, without response, then progressed with cutaneous grayish discoloration. On the next day, she received etanercept 50 mg subcutaneously in a single dose, with excellent clinical response, and no emergence of new lesions or regression of older ones in at least 7 days (FIG. 1c-1d). The corticosteroids were maintained for 7 days.

SSJ/TEN is considered a T cell mediated disorder causing apoptosis of the keratinocytes mediated by tumor necrosis factor alpha (TNF- α). Evidence shows that the concentration of TNF-α in serum blister fluid of patients with SSJ/TEN is elevated and can be noticeably reduced after TNF-α inhibitor treatment alongside with important and rapid resolution of the skin condition, which indicates and supports TNF- α inhibitors such as etanercept as a potential therapy for treating SSJ/TEN [1,2].

Recent studies have shown that allopurinol can induce keratinocyte apoptosis, leading to skin and mucosal lesions such as SSJ/TEN [3]. The reactions typically occur in the first weeks after starting allopurinol [4]. The literature recommends the importance of rapid discontinuation of the drug and immediate initiation of supportive care [4]. A recent Cochrane review comparing etanercept (25 mg - 50 mg if weight>65 kg- twice weekly "until skin lesions healed") versus corticosteroids (intravenous prednisolone 1 to 1.5 mg/kg/day) "until skin lesions healed" concluded with low certainty of evidence that that etanercept group may result in a reduction in mortality [5]. Another study in 2023 showed that etanercept significantly reduced hospitalization [2].

The diagnosis of TEN was made based on her clinical characteristics and histopathological findings. Although the administration of methylprednisolone inside the hospital, the patient's condition did not improve. After the etanercept, a significant clinical improvement was observed in only two days. No side effects were reported. Until now, there has been good recovery, with only scar tissue remaining on the ocular membrane, which in turn maintains follow up with the ophthalmologist. The treatment of SSJ/TEN remains a clinical challenge, and there is a need for more studies with high-level evidence to provide answers and protocol strategies for the benefit to the patients [5]. Drugs that promote a rapid response with a low risk of infection may be a safe and effective option for the treatment of TEN, if started in a timely manner, before complications occur.

1. Conflict of Interest

The authors declare no conflict of interest.

2. Financial Support

This study was conducted without any financial support or funding.

3. Patient consent

The patient in this case report has given written informed consent and accepted to be part of the publication of her case details.

4. Acknowledgement

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