Allopurinol-Induced Toxic Epidermal Necrolysis

Ignacio Buenrostro-Rubio¹ · José Antonio Silva-Villaseñor² · Avi William Hatami-Blechner² · Juan J Salazar-del Valle² · Norma Alejandra Vázquez-Cárdenas³ · Lilia Patricia Bustamante-Montes³ · Rafael González-Alvarez³

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Abstract

Toxic epidermal necrolysis (TEN) is an extremely rare condition characterized by separation of dermoepidermal junctions, necrosis, and subsequent detachment of the epidermis over large cutaneous areas. TEN can emerge after exposure to certain medications such as allopurinol, aromatic anticonvulsants, NSAIDs, nevirapine, and antibacterial sulfonamides. There is no standard protocol for TEN, and the therapy of choice varies from one patient to another. Some of these therapies include silver-releasing wraps/dressings, glucocorticoids, antibodies to inhibit Fas-mediated keratinocyte apoptosis, and cyclosporine A. A 35-year-old male with an allergy to antibacterial sulfonamides who was being treated for arterial hypertension and hyperuricemia with captopril and allopurinol, respectively, was admitted to hospital. The patient showed skin detachment affecting approximately 95% of his surface area, including his face, upper and lower extremities, trunk, back, oropharyngeal mucosa, anal mucosa, ocular mucosa, and genital mucosa. Intravenous methylprednisolone at a dosage of 40 mg/day for 7 days along with abrasive cures was found to be an appropriate treatment in this case.

Key Points

Toxic epidermal necrolysis appears after an idiosyncratic reaction to some drugs.

Symptoms appear 3 weeks after drug intake.

Treatment with corticosteroids in this reported case was appropriate and yielded positive results.

Toxic epidermal necrolysis (TEN), also known as Lyell syndrome in honor of Alan Lyell [1], is an extremely rare condition characterized by the separation of dermoepidermal junctions (DEJ), necrosis, and subsequent detachment of the epidermis over large cutaneous areas. At the beginning of

the last century, Stevens–Johnson syndrome (SJS) and TEN were described as two totally different entities. TEN, SJS/TEN, and SJS are differentiated based on the degree of skin detachment. TEN is classified as the detachment of > 30% of the skin, SJS/TEN involves the detachment of 10–30% of the skin, and SJS is associated with the detachment of < 10% of the skin [2]. TEN can occur after exposure to some drugs, including allopurinol, aromatic anticonvulsants, NSAIDs, nevirapine, and antibacterial sulfonamides [3]. The HLA-B*58:01 allele has been identified as a risk factor for allopurinol hypersensitivity; indeed, in some populations, screening for this allele is recommended before prescribing allopurinol [4].

A 35-year-old male who was 183 cm high and weighed 104 kg presented to the clinic. He was allergic

✉ Rafael González-Alvarez
rgonzalez5@hotmail.com

Ignacio Buenrostro-Rubio
ignacio@buenrostro.mx

José Antonio Silva-Villaseñor
joseansilvamd@yahoo.com

Avi William Hatami-Blechner
avi.hatami@edu.uag.mx

Juan J Salazar-del Valle
jjfsalazar@hospitalsanjavier.com

Norma Alejandra Vázquez-Cárdenas
avc200180@yahoo.com.mx

Lilia Patricia Bustamante-Montes
patricia.bustamante@edu.uag.mx

¹ Buenrostro Medical Center, Guadalajara, México

² Hospital San Javier, Guadalajara, México

³ Departamento de Genética y Medicina Genómica, Facultad de Medicina, Coordinación de Ciencias Clínicas, Universidad Autónoma de Guadalajara, Avenida Dr. Ángel Leño 500, Colonia Los Robles, CP 45200 Zapopan, Jalisco, México

to antibacterial sulfonamides and was being treated for arterial hypertension and hyperuricemia with captopril (150 mg daily for nearly 5 months) and allopurinol (100 mg daily for about 3 weeks), respectively. His allergic background to sulfonamides was reported to manifest as a mild urticaria that disappeared after drug removal and without receiving any treatment. He also reported ibuprofen use without specifying intake time or dose. At a medical consultation, the patient presented with mild urticaria, so a 25-mg chloropyramine hydrochloride tablet was administered, and he returned home. The next day, he returned for another medical consultation, where he reported pruritus and little blisters on his trunk, upper extremities, and back. A 20-mg injection of chloropyramine hydrochloride was then administered. At this point, hospitalization was recommended to allow closer monitoring. There was no recovery during the following 2–3 days; indeed, the blisters worsened until they resembled second-degree burns. At day 8, he showed skin detachment across roughly 95% of his total surface area, including his face, upper and lower extremities, trunk, back, oropharyngeal mucosa, anal mucosa, ocular mucosa, and genital mucosa (Fig. 1). A dermatological

consultation confirmed TEN, after which both captopril and allopurinol were both immediately suspended. Despite the unfavorable conditions, there was no skin infection nor renal failure. Due to oropharyngeal mucosal involvement, the patient showed hypoxemia, so oxygen support was required to kept the oxygen saturation above 94% (Fig. 1b). Both his fluid balance and his creatinine remained stable. The patient's severity-of-illness score for toxic epidermal necrolysis (SCORTEN), which can be used to assess the severity of this condition based on seven independent risk factors (age ≥ 40 years, malignancy, tachycardia > 120 bpm, body surface area involved $> 10\%$, serum urea > 28 mg/dL, serum bicarbonate < 20 mEq/L, and serum glucose > 252 mg/dL) [5], is shown in Table 1. The patient recovered favorably after treatment with surgical cleanliness, debridement, specialized wraps/dressings, intravenous methylprednisolone 40 mg/day, ophthalmic lubricant, humectant, cutaneous amoxicillin, and dexamethasone 0.5 mg/day. The skin reepithelialization process is shown in Fig. 2.

TEN usually presents as a symmetrical, confluent erythematous exanthem that initiates on the face and trunk but rapidly migrates across the trunk and extremities. During

Fig. 1 Clinical presentation of TEN. **a** Dark purple macular lesions on back are shown, as well as incipient blister formation on erythematous/violet zones and detachable skin. **b** Oral mucosa was involved

Table 1 Comparison of standard SCORTEN versus patient SCORTEN

Prognostic factor	Standard value	Points	Patient value	Points
Age	≥ 40 years old	1	35 years old	0
Malignancy	Present	1	Present	1
Body surface area involved	$> 10\%$	1	95%	1
Tachycardia	> 120 bpm	1	86 bpm	0
Serum urea	> 28 mg/dL	1	46 mg/dL	1
Serum bicarbonate	< 20 mEq/L	1	24.70 mEq/L	0
Serum glucose	> 252 mg/dL	1	115 mg/dL	0
Total		7		3

Fig. 2 Skin reepithelialization process. **a** on back and trunk. **b** of the oral mucosa

the evolution of TEN, the lesions present detachment of the laminar epidermis, much like a second-degree burn. This was our first TEN case at the medical center since August 2010. The patient was not aware of any family background of TEN. It is complicated to estimate the incidence and mortality rates of TEN within Guadalajara. In this case, allopurinol was the culprit drug. It has been reported that allopurinol frequently induces SJS/TEN in Europe and Israel [6].

Scientific evidence pointing to the optimal TEN treatment is lacking. Many authors recommend cyclosporine A as the sole immunosuppressant, although further trials of this treatment are planned [7]. We initiated TEN treatment with corticosteroids, specifically intravenous methylprednisolone at a dose of 40 mg/day for 7 days. Abrasive cures were also performed, followed by silver-releasing wraps/dressings. Strict contact isolation and timely hemodynamic support were implemented. It should be noted that the patient did not need vasoactive infusion and there were no infectious complications during his stay at the hospital. During the 7 days of the acute phase, the patient received parenteral nutrition and ophthalmic lubrication with sodium cromoglycate 4%. Based on our experience, treatment with corticosteroids was appropriate and yielded positive results. More clinical research in this field is needed in Guadalajara.

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Compliance with Ethical Standards

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Conflict of interest Ignacio Buenrostro-Rubio, José Antonio Silva-Villaseñor, Avi William Hatami-Blechner, Juan J Salazar-del Valle,

Norma Alejandra Vázquez-Cárdenas, Lilia Patricia Bustamante-Montes and Rafael González-Alvarez have no conflicts of interest that are directly relevant to the content of this study.

Ethical approval Not applicable.

Patient consent Written informed consent was obtained from the patient for the publication of this case report and any accompanying images. A copy of the written consent may be requested for review from the corresponding author.

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