Case report

# Toxic epidermal necrolysis associated with the use of lamotrigine and valproic acid

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**Necrólisis epidérmica tóxica asociada al uso de lamotrigina y ácido valproico**

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**Abstract**
**Case Presentation.** A 27-year-old female patient with a history of depression and migraine was prescribed valproic acid and lamotrigine without progressive titration. Subsequently, she developed diffuse erythematous-violaceous lesions, blisters, skin detachment, mucosal involvement, asthenia, and fever. The condition progressed rapidly, affecting 90 % of the body surface area, with a positive Nikolsky sign, leading to a clinical diagnosis of toxic epidermal necrolysis. **Treatment.** The patient was admitted to the Intensive Care Unit, requiring mechanical ventilation and early tracheostomy, along with targeted antibiotic therapy for septic shock of respiratory and urinary origin. The therapeutic approach included intravenous human immunoglobulin, methylprednisolone pulses, specialized dermatological care, nutritional support, thromboembolic prophylaxis, albumin replacement, and multidisciplinary team involvement. **Clinical evolution.** The patient showed a favorable course, with progressive resolution of mucocutaneous lesions, allowing for decannulation and discharge from the Intensive Care in stable condition. This case highlights the critical importance of gradual titration of lamotrigine, particularly when combined with valproic acid, as well as the relevance of early diagnosis and timely multidisciplinary management in improving the otherwise poor prognosis associated with toxic epidermal necrolysis.

**Keywords**
Near Miss, Healthcare, Anticonvulsants, Lamotrigine, Valproic Acid.

**Resumen**
**Presentación del caso clínico.** Una mujer de 27 años, con antecedente de depresión y migraña, a quien se le prescribe ácido valproico y lamotrigina sin titulación progresiva. Después de 16 días del uso de ambos medicamentos presentó lesiones eritemato-violáceas difusas, ampollas y desprendimiento de la piel, compromiso de mucosas, astenia y fiebre. El cuadro evolucionó rápidamente con afectación del 90 % de la superficie corporal y signo positivo de Nikolsky, por lo que se consideró el diagnóstico de necrólisis epidérmica tóxica. **Intervención terapéutica.** Fue ingresada a la Unidad de Cuidados Intensivos con necesidad de ventilación mecánica, traqueostomía temprana y antibioticoterapia, dirigida por choque séptico de foco respiratorio y urinario. El abordaje terapéutico incluyó inmunoglobulina humana intravenosa, pulsos de metilprednisolona, cuidados dermatológicos especializados, soporte nutricional, profilaxis tromboembólica, reposición de albúmina y la intervención de un equipo multidisciplinario. **Evolución clínica.** La evolución fue favorable, con resolución progresiva de las lesiones mucocutáneas, logró ser decanulada y egresada de Cuidados Intensivos en condiciones estables. Este caso realza la importancia de la titulación progresiva de lamotrigina, especialmente en combinación con ácido valproico, además de la relevancia del diagnóstico precoz y el manejo multidisciplinario oportuno para revertir el pronóstico desfavorable que se asocia a la necrólisis epidérmica tóxica.

**Palabras clave**
Potencial Evento Adverso, Anticonvulsivante, Lamotrigina, Ácido Valproico.

## Introduction

Adverse skin reactions to medications, also known as drug reactions, are manifestations resulting from the systemic administration of drugs. These reactions range from mild erythematous skin lesions to much more serious reactions such as Stevens-Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN). Reactions to certain medications are the most common cause of TEN, and antiepileptic drugs are a subgroup of drugs highly associated with this disease.[i,ii,iii] TEN is rare (incidence of 0.4 to 1.9 cases per million inhabitants per year);[iii] however, its mortality rate is high (30 % of cases).[i, ii, iii]

The pathogenesis of TEN is not fully understood; however, the relationship between these toxicodermias and a type IV hypersensitivity response mediated by T cells is considered. It is postulated that the reaction is initiated by an immune response, in which an antigen-drug-host tissue complex is formed.[iv]

TEN causes detachment of the skin and mucous membranes in more than 30 % of cases. Damage to the skin predisposes to infections and fluid loss, and involvement of the mucous membranes can lead to gastrointestinal bleeding, respiratory failure, ocular abnormalities, and genitourinary complications.[ii] One tool for assessing disease severity and predicting mortality is the SCORTEN scale, which contains seven variables assessed within the first 24 hours of hospital admission. These variables include age > 40 years, heart rate ≥ 120 beats per minute, presence of cancer or hematological neoplasia, affected body surface area ≥ 10 % on the first day, serum BUN > 28 mg/dL, serum bicarbonate < 20 mEq/L, and serum glucose > 252 mg/dL.[i]

TEN is associated with systemic changes and its treatment must be conducted by a multidisciplinary team composed of specialists in intensive care, plastic surgery, dermatology, ophthalmology, among others.

The objective of this study is to describe a case of toxic epidermal necrolysis secondary to the concomitant use of valproic acid and lamotrigine without progressive titration, to highlight the importance of recognizing the drug interaction between them, as well as the need for early diagnosis and timely multidisciplinary management to improve the prognosis of a condition with high morbidity and mortality.

## Case presentation

A 27-year-old woman with a history of migraine and major depressive disorder, who 25 days prior to her hospital admission began treatment with 500 mg of valproic acid daily, to which 100 mg of lamotrigine daily was added nine days later, as part of a therapeutic regimen aimed at symptomatic control of migraine.

After 16 days of combined treatment, she began to experience nonspecific symptoms including general malaise, fever, rhinorrhea, ocular erythema, a foreign body sensation in the oropharynx, and erythematous, pruritic lesions on her lower limbs.

Given the initial suspected diagnosis of mild dengue, she received analgesic treatment with paracetamol (two 500 mg doses) and loratadine was prescribed for the pruritus; however, she showed no clinical improvement. The condition progressed rapidly with the appearance and spread of vesicles, petechiae, and generalized pruritus. It was associated with facial edema, dysphagia, odynophagia, blistering, and whitish lesions on the oral and genital mucosa, consistent with extensive mucocutaneous involvement.

The patient was admitted to the Intensive Care Unit (ICU) due to the imminent risk of airway compromise, with a high probability of requiring mechanical ventilation and the need for invasive monitoring.

Upon admission to the ICU, erythroderma was observed. Facial edema, desquamation in the malar, nasal, and chin regions, tense blisters on the auricles, conjunctival hyperemia, chemosis, and purulent discharge suggestive of bacterial superinfection were observed on the head.

The nasal mucosa showed intense erythema and desquamation at the entrance to the nostrils. In the oral cavity, cheilitis with significant labial edema, vesicles on the gums and hard palate, coated tongue, and diffuse erythema of the oropharynx were observed (Figure 1).

In the anterior and posterior thoracic region, abdomen, and lumbar region, rounded erythematous-violaceous macules and papules were observed, scattered with a tendency to coalesce, as well as blisters with serous content, with a diameter of two cm to five cm (Figure 2).

In the genitourinary region, she presented with edema and erythema in the vulva and leukorrhea. In the sacral region, there was desquamation, while isolated erythematous-violaceous macules and papules were observed on the extremities.

In the complementary tests, serology was performed for cytomegalovirus infection, hepatitis B and C, and herpes I and II, all of which were negative; VDRL and HIV 1+2 were non-reactive. Table 1 describes the laboratory findings upon admission, on the eighth day, and upon discharge from intensive care.

## Treatment

Extensive hydration with Ringer's lactate (at 2 ml/kg/h = 3120 ml in 24 hours) and analgesia with morphine at 1.6 mg/h were instituted.

The patient was evaluated by dermatology, plastic surgery, gynecology, and ophthalmology. Dermatology indicated treatment with human immunoglobulin at a dose of 4.6 g/day for five days. She received methylprednisolone pulses (three 500-mg doses), followed by oral prednisone

(1 mg/kg), starting at 60 mg and gradually decreasing to 10 mg/day. Plastic surgery indicated healing lesions using sterile material, saline solution, and vaseline gauze. The use of soap solutions was omitted, and biocompatible dressings were not used due to a lack of resources at the institution. She received ophthalmic treatment with tobramycin, dexamethasone, artificial tears, and ophthalmic protection (occlusion). Gynecology indicated the administration of clotrimazole and metronidazole ovules (for five days). Prophylactic anticoagulation was instituted with enoxaparin at a dose of 40 mg daily, and enteral nutritional support was initiated via nasogastric tube, with a progressive increase in calories until reaching a target of 1800 kcal. Complementary tests on subsequent days revealed hypoproteinemia (4.90 g/dL) with hypoalbuminemia (2.26 g/dL), for which 20 % human albumin was prescribed for three days.

**Figure 1.** Erythroderma, facial edema, skin peeling, and cheilitis.

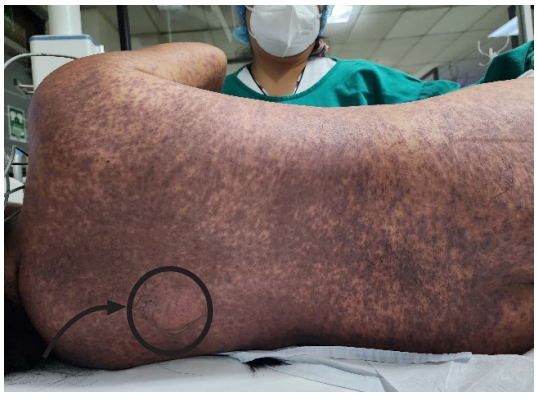

**Figure 2.** Lesions in the posterior thoracic region, disseminated erythematous-violaceous lesions, and areas of skin detachment (arrow).

**Table 1.** Complementary Laboratory Tests on Admission, Day 8th of Hospitalization, and at ICU Discharge

| Reference values | Day 1 | Day 8 | Day 16 |
|---|---|---|---|
| Leukocytes: 4.500-10.000 x$10^3$ µL | 7.000 x$10^3$ µL | 12.000 x$10^3$ µL | 11.070 x$10^3$ µL |
| Neutrophils: 2.200-4.800 x$10^3$ µL | 6.000 x$10^3$ µL | 8.460 x$10^3$ µL | -8.050 x$10^3$ µL |
| Lymphocytes: 1.100-3.200 x$10^3$ µL | 0.72 x$10^3$ µL | 1.89 x$10^3$ µL | 1.99 x$10^3$ µL |
| Eosinophils: 0.0 – 0.70 x$10^3$ µL | 0.320 x$10^3$ µL- | 0.05 x$10^3$ µL | 0.06 x$10^3$ µL |
| Platelets: 130 – 400 x$10^3$ µL | 210.000 x$10^3$ µL | 304.000 x$10^3$ µL | 618.000 x$10^3$ µL |
| Hemoglobin: 14 – 18 g/dL | 13.3 g/dL | 8.2 g/dL | 10.8 g/dL |
| Hematocrit: 42- 52 % | 38.80 % | 26.50 % | 32.30 % |
| Sodium (Na): 135-155 mmol/L | 140.7 mmol/L | 142 mmol/L | 141 mmol/L |
| Potassium (K): 3.35- 5.50 mEq/L | 3.68 mEq/L | 4.03 mEq/L | 3.51 mEq/L |
| Chloride (Cl): 94 – 110 mmol/L | 112 mmol/L | 103 mmol/L | 104 mmol/L |
| Urea: 10 – 50 mg/dL | 9 mg/dL | 40 mg/dL | 20 mg/dL |
| Creatinine: 0.70- 1.20 mg/dl | 0.9 mg/dL | 0.45 mg/dL | 0.34 mg/dL |
| AST: 10-32 U/L | 106 U/L | 23 U/L | 38 U/L |
| ALT: 10- 33 U/L | 203 U/L | 48 U/L | 28 U/L |
| GGT: 5.0 – 36 U/L | 75.1 U/L | 75.1 U/L | 51 U/L |
| LDH: 135 – 225 U/L | 390 U/L | 156 U/L | 156 U/L |
| Alkaline Phosphatase: 0-270 U/L | 77 U/L | 137 U/L | 134 U/L |
| Total Protein: 6.60- 8.7 g/dl | 5.17 g/dL | 4.9 g/dL | 5.9 g/dL |
| Albumin: 3.50 - 5.50 g/dL | 3.36 g/dL | 2.26 g/dL | 3.26 g/dL |
| Total Bilirubin: 0.0 – 1.20 mg/dL | 0.18 mg/dL | 0.25 mg/dL | 0.22 mg/dL |
| Direct Bilirubin: 0.0 – 0.29 mg/dL | 0.10 mg/dL | 0.15 mg/dL | 0.13 mg/dL |
| Indirect Bilirubin 0.0 – 0.70 mg/dL | 0.08 mg/dL | 0.10 mg/dL | 0.09 mg/dL |

## Clinical evolution

Upon admission, the patient had adequate ventilatory mechanics, with pulse oximetry saturation above 90 % with supplemental oxygen support via nasal cannula $FIO_2$: 24 %; However, on the third day, she presented respiratory deterioration due to significant airway edema, use of accessory muscles, and poor management of secretions with pharyngeal lake or pharyngeal residue, for which orotracheal intubation and mechanical ventilation were decided. During laryngoscopy, significant airway edema was observed, Cormack IV. She was connected to volume-controlled mechanical ventilation, and sedoanalgesia was initiated with midazolam and fentanyl.

On the eighth day of hospitalization, a fibrobronchoscopy was performed, revealing tracheal edema, thickening of the carina, shortening and edema of the left bronchus, and edema of the right bronchus. For this reason, a percutaneous tracheostomy was performed (Figure 3).

Due to blood loss attributed to her injuries, she presented a decrease in hemoglobin to 8 g/dL, requiring transfusion support with a red blood cell concentrate.

During her stay in intensive care, she presented hemodynamic decompensation associated with septic shock of urinary and pulmonary origin (ventilator-associated pneumonia). A culture of tracheal aspirate isolated *Acinetobacter baumannii* plus multiresistant *Staphylococcus aureus*, and a urine culture isolated *Escherichia coli* plus multiresistant *Proteus mirabilis*. Antibiotic therapy with ampicillin plus sulbactam and cefepime was initiated for seven days.

The patient was weaned off mechanical ventilation after 15 days of hospitalization and decannulated on the 17th day after her admission to the ICU. She tolerated oral feeding well.

She was discharged after 18 days of hospitalization with substantial clinical improvement. Exfoliation of the skin on the face, chest, and extremities was observed, with no edema on the face, mild erythema, blistering lesions in the process of healing, and no signs of inflammation (Figure 3 and Figure 4).

## Clinical diagnosis

The skin peeling was progressive, and on the third day of hospitalization, it involved 90 % of the body surface, with a positive Nikolski sign (Figure 5). The diagnosis of toxic epidermal necrolysis was based on the history of drug exposure to the aforementioned anticonvulsants and their etiopathogenic link to this condition, as well as the correlation between drug administration and the development of signs and symptoms.

For prognostic stratification, the SCORTEN scale was used, in which three positive criteria were found: tachycardia (heart rate of 132 beats per minute), reduced serum bicarbonate(18 mmol/L), and total body surface area involvement greater than 10 %.

## Discussion

Migraine prophylaxis aims to reduce the frequency, intensity, and duration of episodes, especially in patients with recurrent or incapacitating attacks. Conventional treatments such as antihypertensives, antiepileptics, and antidepressants are widely used in daily practice. However, their efficacy is variable due to nonspecific mechanisms of action and adverse effects that may limit their tolerability.[v]

Valproic acid continues to be one of the drugs with the strongest scientific backing in migraine prophylaxis, with level A recommendations supported by controlled clinical trials, systematic reviews,

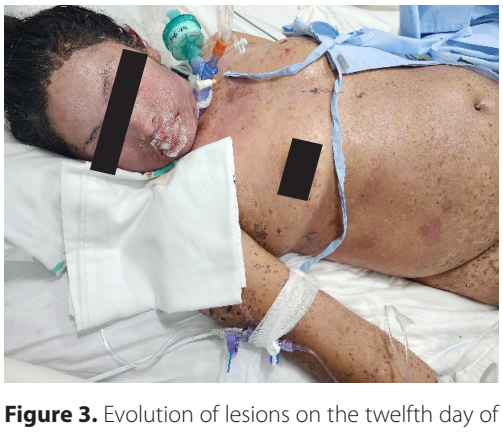

**Figure 3.** Evolution of lesions on the twelfth day of hospitalization. Exfoliation of the skin on the face and chest, and resolution of erythema are observed.

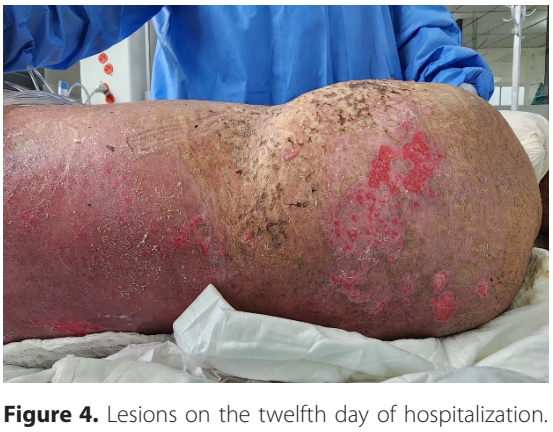

**Figure 4.** Lesions on the twelfth day of hospitalization. Areas of skin abrasion due to deeper skin peeling are observed in the gluteal region (pressure area).

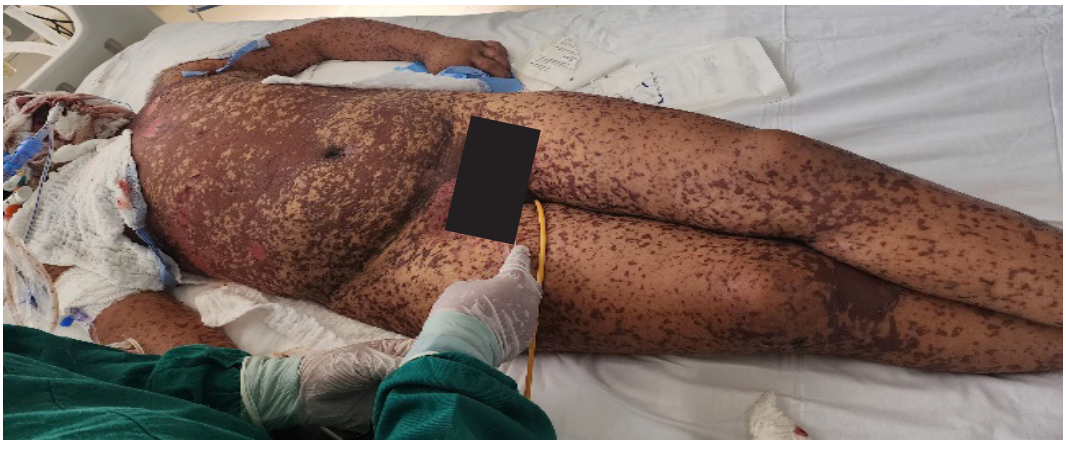

**Figure 5.** The affected area, which covers 90 % of the body surface, is detached.

and meta-analyses, which show a significant reduction in the frequency of episodes and good tolerability.[vi,vii]

In contrast, lamotrigine has shown limited efficacy as a prophylactic agent in controlled studies, so its routine use for this purpose is not recommended.[viii] Although some anticonvulsants, such as gabapentin, pregabalin, levetiracetam, and carbamazepine, have shown partial benefit in certain contexts, the current evidence remains insufficient to support their systematic use in the prevention of migraine.[v] The combined use of these antiepileptics in the prevention of migraine is not supported by the literature, and their use could increase the development of adverse events such as TEN. In this patient, the combination of valproic acid and lamotrigine was used for the prophylactic management of migraine. However, there is no clear information as to whether the psychiatrist's indication for lamotrigine was due to the presence of a concomitant mood disorder.

TEN is a potentially fatal disorder characterized by detachment of the skin and mucous membranes.[ii] Its most common etiology is an adverse reaction to drugs. According to the 2008 Euro-SCAR study, drugs with a potential risk of TEN are anticonvulsants, especially lamotrigine.[i] Several studies report that the combination of lamotrigine and valproic acid can trigger severe toxicodermias such as SJS and TEN.[ix-xii]

A meta-analysis conducted by Rashid *et al.*, found that of a total of 21 patients with TEN/SJS, all were exposed to valproic acid, of whom even received the drug as monotherapy, while the rest were undergoing concomitant treatment with another anticonvulsant medication, the main reason is the interference of valproic acid with metabolizing proteins in the liver.[xiii] Lamotrigine is mainly metabolized by hepatic glucuronidation, by the enzymes UGT1A4 and UGT2B7. Valproic acid inhibits these enzymes, significantly reducing the clearance of lamotrigine by more than 50 %[xiv] and prolonging its half-life to 30 to 60 hours, which increases its systemic concentrations.[xiii]

The sustained increase in plasma levels of lamotrigine, due to the inhibition of metabolism by valproate, is linked to an increased risk of serious skin reactions such as TEN. It has been noted that this interaction not only decreases the clearance of lamotrigine but also redirects its metabolism to alternative pathways that generate reactive metabolites, potentially toxic and related to cellular sensitization, thus establishing a pharmacokinetic basis for increased skin risk.[xv]

Given the known pharmacokinetic interaction between lamotrigine and valproic acid, a gradual titration regimen is recommended. This consists of starting with 25 mg of lamotrigine every 48 hours for the first two weeks, followed by 25 mg daily for the next two weeks.[xii,xiii]

However, in the clinical case presented, an initial dose of 100 mg daily of lamotrigine was administered in combination with 500 mg daily of valproic acid, omitting the recommended titration phase. This accelerated administration may have caused early accumulation of the drug, promoting the development of a severe adverse skin reaction.

There is no laboratory test to confirm a specific pharmacological etiology;[xvi] however, a causal link is suggested when TEN occurs during the first four weeks of treatment with suspect medications. TEN mimics a delayed hypersensitivity reaction to initial exposure and an increasingly rapid reaction with repeated exposures. Generalized epidermolysis and blistering in TEN are the result of keratinocyte apoptosis, with an organized series of biochemical reactions leading to cellular changes and cell death.[i]

Skin involvement in TEN is preceded by a prodromal period that may include fever, cough, rhinorrhea, conjunctivitis, and asthenia. It generally occurs between one and three weeks after exposure to the drug. Signs on the mucous membranes (eyes, mouth, nose, and genitals) begin after the prodrome in 90 % of cases.[iii] The skin lesion is characterized by a poorly defined dark erythematous macular rash, which converges to form blisters that can easily detach, leaving the dermis exposed and moist.[i] The skin and posterior mucosal involvement are diffuse and usually appear as erythematous macules or atypical target lesions on the trunk that progress to become confluent areas of erythema with dark centers, flaccid blisters with a positive Nikolsky sign, and sheets of exposed epidermis. Epidermal detachment is progressive, followed by a variable period of re-epithelialization, usually lasting one to three weeks.[iii]

Mucosal lesions most commonly affect the mouth, throat, eyes, and genitals along with the anus, and less frequently the nose, esophagus, trachea, and bronchi, resulting in dysphagia, genitourinary dysfunction, denudation, difficulty clearing secretions, atelectasis, and acute respiratory failure. In this situation, the patient may require mechanical ventilation and is therefore at risk of developing complications associated with ventilatory support.[iii,iv] Epidermal loss leads to electrolyte imbalance, hypoalbuminemia, impaired body thermoregulation, and an increased risk of infection, resulting in a mortality rate of 50 % for TEN, with the most common causes being sepsis and pneumonia.[xviii]

Treatment of TEN involves recognizing the disorder as early as possible and immediately removing the causative agent. The basis of treatment is supportive care until the epithelium regenerates. Fluid resuscitation should maintain adequate tissue perfusion by achieving an arterial pressure of 6.5 mmHg, a central venous pressure in the range of 8 to 1.2 mmHg, and urine output in the range of 0.5 to 1 ml/kg/hour. A sterile, non-adhesive dressing should be used to cover areas of skin erosion, and care should be taken to prevent hypothermia.[xviii]

Early transfer of patients to intensive care or burn units has been shown to reduce the risk of infection, mortality rates, and length of hospital stay.[i]

Patients with TEN, in addition to intubation, may require early tracheotomy (before day ten on mechanical ventilation), especially if there is involvement of the oral mucosa and an initial body surface area of 70 %. Caloric requirements are increased in TEN, so an intake of 30 to 35 kcal/kg is indicated. Nutritional support is essential in patients with TEN due to the hypercatabolic nature of the condition. Enteral nutrition is superior to parenteral nutrition, due to its reduced risk of bacterial translocation. Enteral nutrition is preferable to prevent the formation of stress ulcers and infectious complications. Pain management should be individualized according to the patient's pain level and comorbidities. Therapy with intravenous bolus or infusion of morphine or fentanyl is indicated if the pain is severe. Due to the increased risk of venous thromboembolism in patients with TEN, prophylaxis with low molecular weight heparin is recommended.[xix]

Regarding the specific treatment of the disease, there is evidence that pulses of methylprednisolone reduce levels of proinflammatory cytokines such as interferon gamma, tumor necrosis factor (TNF) alpha, and interleukin-6 (IL-6); however, their use is controversial, since the administration of corticosteroids can prolong hospital stays due to the increased risk of infections.[xvii,xx,xxi] Although corticosteroids pose a risk in terms of delaying skin regeneration or immunosuppression in patients, their administration for short periods and with gradual reduction in dosage could be a useful strategy for interrupting the inflammatory cascade associated with massive keratinocyte apoptosis.[xxii]

There is also information supporting the use of human immunoglobulin, whose usefulness is based on its protective effect on keratinocytes, thereby limiting the progression of the disease. Some authors indicate that its efficacy is increased with the administration of methylprednisolone, improving short- and medium-term complications with a dose of 1 g/kg of immunoglobulin and 1 g of methylprednisolone, both for three to five days.[xvii,xx,xxii]

When comparing the clinical case presented with the findings of a series of eight cases of TEN in Japan, conducted by Sakai *et al.*, both therapeutic similarities and relevant clinical differences were observed.[xxiii] In the aforementioned study, all patients affected by TEN were over 40 years of age. The majority had comorbidities, and the only known survivor, who was discharged at 43 years of age, had no concomitant diseases. In contrast, the patient in this case was younger and had no comorbidities.[xxiii] In all cases in the study conducted by Sakai *et al.*, there was an indication for orotracheal intubation with mechanical ventilation to protect the airway, with a range of a few days from admission to mechanical ventilation to intubation of one to six days; similarly, the patient described required invasive mechanical ventilation on

the third day of admission to the ICU. The pharmacological treatment was based on the use of systemic corticosteroids, intravenous immunoglobulin, sedation (although with different regimens: midazolam in our case, propofol exclusively in the Japanese study), and analgesia with fentanyl.

Most patients with TEN develop complications due to infections that often culminate in septic shock. The barrier function of the mucocutaneous is altered, and the immune system is suppressed by the use of corticosteroids.[xxiii] Invasive mechanical ventilation and the use of a urinary catheter increase aggression to the mucosa, which, added to the factors mentioned above, favored the development of respiratory and urinary tract infections in the patient in this clinical case. In the Japanese study in question, all patients progressed to multiple organ failure. In contrast, the clinical evolution of the case presented involved septic shock of urinary and respiratory origin, but did not result in established multiple organ failure. The younger age of the patient could explain this difference, along with the absence of comorbidities and the early implementation of critical support measures and targeted antibiotic therapy.

Despite the severity of the patient's clinical condition, her stay in the ICU was comparable to that of the only patient discharged in the case series, suggesting that early intensive intervention can modulate the prognosis, even in patients with high SCORTEN scores.

## Ethical aspects

The established guidelines for ethical research involving human subjects and the Declaration of Helsinki were followed; informed consent was obtained from the patient's legal representative (mother) and subsequently from the patient herself for the use of clinical data and publication, and the bioethical principles of privacy and confidentiality were respected.

## Conclusion

The combination of valproic acid and lamotrigine lacks support in the literature for the prophylactic treatment of migraine, and poses a potential risk of adverse reactions, such as toxic epidermal necrolysis, which occurred in the patient in this case report. This highlights the importance of appropriate prescribing of anticonvulsants and individual assessment of the benefit-risk profile of each drug, especially when valproic acid and lamotrigine are combined. It also highlights the need for early recognition of the clinical picture, immediate withdrawal of the causative agent, and comprehensive management in the ICU. The absence of progressive titration of lamotrigine, initiated at high doses and in concomitance with valproic acid, favored the onset of TEN, an adverse reaction. This combination enhances skin toxicity because valproate inhibits the hepatic metabolism of lamotrigine, significantly increasing its half-life and serum concentration.

Early diagnosis and timely multidisciplinary intervention, using intravenous immunoglobulin, corticosteroid pulses, ventilatory support, targeted antibiotic therapy, thromboembolic prophylaxis, and nutritional support, were decisive in reversing an initially unfavorable prognosis.


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