

Severe cutaneous reactions caused by barbiturates in seven Iranian children

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Abstract

Background The severe adverse cutaneous reactions of erythema multiforme (EM), Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare mucocutaneous diseases associated with significant morbidity and mortality. The most common cause is antiepileptic drugs, particularly carbamazepine and lamotrigine, as well as the barbiturates group (phenobarbital and phenytoin). In this article, we present seven children with severe adverse cutaneous reactions caused by barbiturates.

Case Reports The age of the affected children was between 2 and 11 years and they all had a history of taking barbiturates. Their symptoms started 1–3 weeks after the initiation of barbiturates, including a prodrome characterized by 2–3 days of malaise, fever, cough and anorexia, after which the skin and mucosal lesions appeared and worsened. The skin lesions varied from rash to large bullae, plus different forms of mucous membrane involvement. The offending drugs (barbiturates) were stopped immediately and care was largely supportive.

Conclusion As a result of the morbidity and/or mortality associated with EM, SJS and TEN, physicians should keep in mind their differential diagnosis when cutaneous reactions are observed in patients undergoing barbiturate therapy. Furthermore, although TEN and SJS are life-threatening diseases, early detection and appropriate care can lead to a decrease in the incidence of death. The strategies described here seem to be successful and safe because, despite the serious conditions, our patients responded well. All survived.

Introduction

Severe adverse cutaneous reactions, including erythema multiforme (EM), Stevens–Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN), are mucocutaneous diseases associated with significant morbidity and mortality.¹ These three cutaneous eruptions can all be caused by drug therapy; EM and SJS also have many causes unrelated to drug therapy.² Other etiologies include infections, radiotherapy, malignancies (lymphoma and leukemia), and vaccinations (diphtheria, poliomyelitis, and measles).³ These diseases can occur in association with more than 100 different medications, including some commonly used antiepileptic drugs, particularly carbamazepine, lamotrigine, phenobarbital, and phenytoin (belonging to the barbiturates group).⁴ The annual incidence of EM has been estimated to be between 0.01 and 1%; the incidences of SJS and TEN have been estimated to be 0.4–1.2 and 1.2–6 per million person years, respectively.^{1,2} EM is a characteristic cutaneous hypersensitivity reaction characterized by an erythematous

eruption, with the development of target-like iris lesions, sometimes with bullae, symmetrically on the extensor surfaces of the extremities, palms, and soles. In EM major, in addition to the acral eruption, the mucosal surfaces are affected.³ SJS is characterized by mucous membrane erosions and blisters on limited areas of skin (< 10% of the total body surface area), TEN, first referred to as Lyell's syndrome in 1956, is a severe, acute, potentially life-threatening mucocutaneous disease that affects almost every system of the body.^{5,6} It resembles superficial burns because of the confluence of blisters and erosions on more than 30% of the total body surface area.⁷ TEN is characterized by extensive blistering of the skin with full-thickness necrosis of the epidermis, as in second-degree burns, and mucosal involvement. Skin detachment occurs at the dermo-epidermal junction, and gives the skin a typical “wet dressing” appearance; the epidermis can be removed easily by light tangential pressure (Nikolsky's sign).^{8,9} Universal involvement of the mucous membranes varies according to the level of involvement in each area (eyes, mouth, airway, esophagus, rectum,

vagina, and urethra), but commonly affects the oral cavity.^{8,10,11} Initially, only the face and trunk are affected, but, as the condition progresses, the lesions become generalized.¹⁰

The mortality from SJS and TEN has been estimated to be 5–15% and 25–30%, respectively, with secondary sepsis being a frequent cause of death,^{9,11} but mortality from EM is very rare.¹ Age, percentage of denuded skin, neutropenia, serum urea nitrogen level, and visceral involvement are prognostic factors.¹⁰

The standard management of severe adverse cutaneous reactions includes discontinuation of treatment with the suspected causative drug, fluid replacement including colloids, strict intake and output, use of nonstick dressings soaked with normal saline or 0.5% silver nitrate, control of infection and sepsis, nutritional therapy, pain management, and, recently, intravenous immunoglobulin (IVIG).⁷

In this article, we present seven children admitted to the Children Medical Center in Tehran, Iran, with severe adverse cutaneous reactions (EM, SJS, and TEN) caused by barbiturate consumption, and the treatment strategies during 2004–05.

Case reports

Case 1

A 5-year-old boy was referred to the Department of Infectious Diseases with a differential diagnosis of staphylococcal septicemia or Kawasaki disease. On admission, he showed a generalized macular erythematous eruption (Fig. 1), fever and shaking chills, malaise, anorexia, and pharyngitis. He also complained of painful bilateral lymphadenopathy in the neck. The patient had a history of nonproductive cough and abdominal pain without nausea and vomiting of 7 days' duration. The patient had been treated with phenobarbital



Figure 1 Widespread epidermal loss over the body surface seen 5 days after discontinuation of phenobarbital in a 5-year-old boy with toxic epidermal necrolysis

(5 mg/kg/day) for 2 weeks following a first incidence of seizure. After 10 days of drug therapy, he developed a macular eruption on the face which, in a short time, extended to the trunk and extremities. He had not received any over-the-counter drugs, herbal or naturopathic medications.

On examination, the patient was febrile, ill, and toxic. Vital data revealed a respiratory rate of 30/min, a pulse rate of 130/min, a blood pressure of 70/40 mmHg, and a temperature of 39 °C. His body weight was 16 kg. The skin showed a maculopapular eruption with confluent erythema affecting the body surface area. There was erythema in the pharynx and lymphadenopathy (1.5 × 2 cm in diameter) bilaterally in the neck with tenderness. The patient showed normal respiratory auscultation, but tachycardia on cardiovascular examination. On abdominal examination, there was tenderness in the right upper quadrant without organomegaly.

Initial laboratory tests included a white cell count of $5.2 \times 10^9/L$ [normal range (NR), $(4.0-11.0) \times 10^9/L$], hemoglobin of 9.8 g/dL (NR, 13–17 g/dL), and erythrocyte sedimentation rate (ESR) of 32 mm/first hour (NR, 0–20 mm/h). Renal function tests and blood gases were normal. Serum liver enzymes were abnormal with an elevated aspartate aminotransferase (AST) of 181 U/L (NR, 0–46 U/L) and alanine aminotransferase (ALT) of 128 U/L (NR, 0–49 U/L). Serum albumin was 3.3 mg/L (NR, 3.5–5.5 mg/L), C-reactive protein (CRP) was positive (++) (20 mg/L), and the prothrombin time (PT) was 15.2 s (control, 13 s) on admission. Other laboratory test results were within normal limits initially.

Chest radiography revealed bilateral parahilar opacities and an increase in thickness in the peribronchial area. In abdominal sonography, the spleen, liver, and biliary tract were reported to be normal, but ascites was seen. In renal sonography, the echo of both kidneys was increased. Initially, a diagnosis of phenobarbital-induced SJS was made and phenobarbital was discontinued immediately. The patient was started on supportive care; however, his condition continued to deteriorate and his eruption continued to spread rapidly and, during the following 4 days, involved 70% of the body surface area. The child was disoriented, confused, and somnolent with persistent fever. Furthermore, painful eyes and mouth ulcers appeared. The lesions in the oral mucosa extended and Nikolsky's sign was positive. The mouth and nose showed severe hemorrhagic mucositis, resulting in the loss of one tooth. Some nails were also lost. The mucous membranes of the perineum and perianal regions were also affected. The patient was seen and followed by an ophthalmologist, and marked ocular involvement was noted with bilateral conjunctivitis, photosensitivity, and the presence of bilateral palpebral contraction. A diagnosis of TEN related to phenobarbital was made on the basis of all of the findings. On the fifth day, the eruptions began to rupture and developed desquamation and keratinopathy, and nonpitting edema was detected in the lower extremities. On the following days,

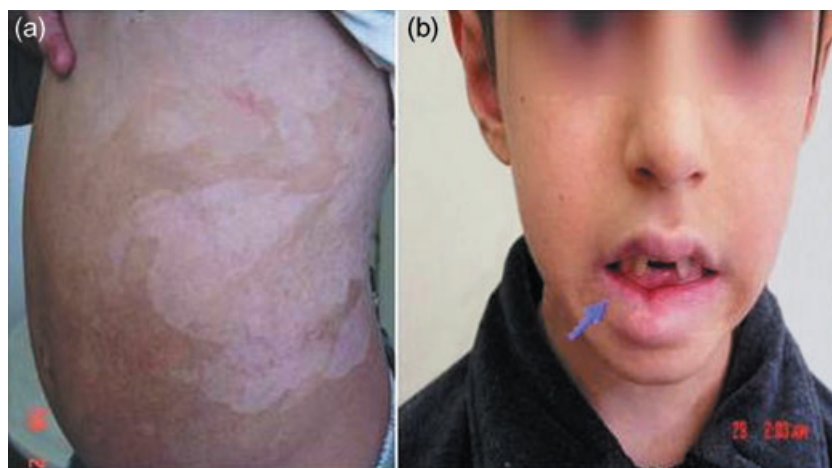


Figure 2 One month after discharge of a 5-year-old boy with toxic epidermal necrolysis: (a) postinflammatory hyperpigmentation at the sites of previous eruption; (b) defect on the lower lip resulting from severe mucous membrane involvement of the mouth

the patient showed salivation, photophobia, dysphagia, and diarrhea. Other observations consisted of hemorrhagic crusting of the lips, and denudation of extensive epithelial areas of the body surface.

The patient was barrier nursed in an isolated room and received treatment and care.

On the seventh day of admission, CRP was positive (++++)(80 mg/L); *Escherichia coli* was found in urine culture and *Acinetobacter* was identified in skin swab and blood cultures. The antimicrobials were adjusted on the basis of the microbiology of the cultures to inhibit the growth of the identified organisms (amikacin, ceftazidime).

During admission, the patient showed complications of the gastrointestinal tract, such as vomiting and diarrhea, that were treated with oral rehydration solution (ORS) (50 cm³ per deification). The patient's lymphocyte count dropped to a nadir of $2.6 \times 10^9/L$ with lymphopenia [$6.5 \times 10^8/L$; NR, $(2.2-7.7) \times 10^9/L$], but increased to within normal limits by the time of discharge (on the 23rd day of admission). Medical care and procedures were continued until wound healing was complete and the patient was close to hospital discharge. After 10 days, the eruptions began to clear. Re-epithelialization of the previously sloughed areas occurred and was complete about 3 weeks later, and the general condition of the patient remained satisfactory. He was discharged after 23 days, by which time the skin had healed with extensive postinflammatory hyperpigmentation. One month after discharge, examination revealed areas of postinflammatory hyperpigmentation at the sites of previous eruption (Fig. 2a) and a defect on the lower lip resulting from severe mucous membrane involvement of the mouth (Fig. 2b). In addition, he showed aggressive behavior and was seen by a psychologist; he remains under observation.

Case 2

A 6-year-old girl was started on phenobarbital, 50 mg twice daily, following generalized convulsions. Two weeks after commencing the drug, she developed a generalized cutaneous

eruption and aphthous ulcers of the mouth without bullae. Four days later she was admitted to hospital with a widespread bullous dermatosis, erythema, and crusted ulcers on the lips. She had not received any over-the-counter drugs, herbal or naturopathic medications. She did not have any history of allergy, but her parents had a history of seasonal allergy.

On examination, the patient was ill, toxic, and febrile. Her temperature was 38 °C, and she had a respiratory rate of 30/min, pulse rate of 110/min, and blood pressure of 100/60 mmHg. Her body weight was 16 kg. Her skin showed erythema affecting the body surface area. She had multiple bullae on the body surface area (Fig. 3). Her mouth showed severe mucositis and crusted ulcers. Nikolsky's sign was positive. There were erosions on the genitalia. On abdominal examination, there was tenderness in the right upper quadrant without organomegaly. Cardiovascular and respiratory examinations were normal. Biochemistry tests and chest X-ray were normal. A diagnosis of TEN was made and phenobarbital was discontinued immediately. She was started on supportive care. She was commenced on IVIG, 1 g/kg daily. Over the first 2 days, there was further epidermal loss, affecting 50–60% of the body surface area. The patient was barrier nursed in an isolated room and was treated. Medical care and procedures were continued until evidence of re-epithelialization appeared. The patient recovered completely and was discharged after 10 days without any problems.

Case 3

A 7.5-year-old boy with generalized cutaneous eruption, painful eyes and mouth ulcers, and malaise was admitted to hospital. He had been started on phenobarbital and cotrimoxazole following brain tumor surgery. Three weeks after commencing these drugs, he developed the cutaneous eruption. He had no history of drug reactions or allergies. His medical history was negative except for the brain tumor.

On admission, he was unable to speak or to take fluids by mouth because of mouth ulcers (Fig. 4). He was in a poor



Figure 3 Multiple large bullae on the leg of a 6-year-old girl with toxic epidermal necrolysis



Figure 4 Eye involvement, severe mucositis, and crusted ulcers in a 7.5-year-old boy with toxic epidermal necrolysis



Figure 5 Generalized ecchymotic and petechial eruptions, crusts, and blisters on admission in a 7.5-year-old boy with toxic epidermal necrolysis

condition and his vital signs revealed a pulse rate of 92/min, a respiratory rate of 34/min, and a temperature of 37.2 °C. His weight was 23 kg. He had generalized ecchymotic and petechial eruptions, crusts, and blisters (Fig. 5). On the extremities, there were patchy, bullous, and ecchymotic lesions, with some confluent blisters and sheets of skin separated in these areas. He reported considerable pain from severe genital lesions. On auscultation, there were rales in the lungs. Cardiovascular examination was normal. The abdomen was distended but nontender.

It was estimated that approximately 30% of the skin was eroded. Initial laboratory tests showed a hemoglobin of 11.6 g/dL, a total white cell count of $8.8 \times 10^9/L$, with 8% eosinophils, and a platelet count of $297 \times 10^9/L$. The ESR was 32 mm in the first hour. Renal function tests and blood gases were normal. Urinalysis and blood chemistry [fasting blood glucose, Na, K, blood urea nitrogen (BUN), creatinine] were normal. Urine and blood cultures were negative and chest radiography was normal.

A diagnosis of TEN was made and anticonvulsant therapy was discontinued immediately. The patient was isolated in a heated room and treatment was performed. Ten days after admission, there was evidence of re-epithelialization. He was discharged with the parent's consent.

Case 4

A 2-year-old, previously healthy, boy with a febrile convulsion was treated with phenobarbital, 15 mg (2.5 tablets daily), for 8 days before admission. On admission, he had fever, cough, and chilling, and 1 day later developed bullae that started at the eyelid and worsened, with numerous brown macules on the trunk and limbs, and, in the following few days, erythema, malaise, and sore mouth, lips, and eyes. He had a history of

one incidence of melena 2 days earlier. He had no previously known drug allergies, and no medication consumption history except for phenobarbital. His past medical and family histories were noncontributory.

On admission, he was febrile (temperature, 38.5 °C), but nontoxic, with a pulse rate of 124/min and respiratory rate of 22/min. His weight was 12 kg. On examination, he had an extensive, generalized, maculopapular eruption, crusts, and blisters, with separation of sheets of skin in areas in which the blisters had become confluent. He had white sores on the palate. Nikolsky's sign was positive. There were patchy erythematous lesions on the extremities. The genitalia were also involved.

On auscultation, there were crackles in the right lung and wheezing in the left. Cardiovascular and abdominal examinations were normal.

Laboratory evaluations found a leukocyte count of $8.3 \times 10^9/L$ and hemoglobin of 11 g/dL. The ESR was 32 mm/h. Liver enzymes and urinalysis were normal. He had mild albuminuria. Serum chemistry was normal, and urine and blood cultures were negative. Chest radiography was normal.

A diagnosis of SJS/TEN was made and discontinuation of phenobarbital was performed immediately and treatment was begun. His symptoms progressively resolved in 8 days. He was discharged home without any sequelae.

Case 5

An 11-year-old girl was admitted with a 3-day history of an erythematous eruption on the face and neck that had worsened. Her medical history included a convulsion 2 months earlier that was treated with phenobarbital, 5 mg/kg/day; however, because of side-effects (dizziness), phenobarbital was changed to carbamazepine 15 days before admission. Her family history included asthma in her grandfather. She gave no history of the recent use of other medications. On examination, she was afebrile. Her respiratory rate was 23/min, pulse rate 90/min and blood pressure 100/50 mmHg. She was not ill or toxic. On skin examination, generalized erythematous papules and targetoid lesions with petechia and purpura were seen. Gradually, blisters appeared. Mouth sores occurred and she could not speak because of pain. There were conjunctival and genital erosions. The abdomen was nontender with no organomegaly. Laboratory examination found a leukocyte count of $6.7 \times 10^9/L$, hemoglobin of 12 g/dL, and platelet count of $194 \times 10^9/L$. Other biochemical results were within normal limits initially. Urinalysis was normal. Blood and urine culture were negative. Her chest radiograph was normal. Based on the chemical findings, she was diagnosed with SJS and the anticonvulsive medication was discontinued. With treatment and medical care, her symptoms progressively resolved and she was discharged home after 5 days.

Case 6

A 4-year-old girl was started on phenobarbital, 15 mg three times daily, following a first incidence of seizure. One week after commencing this drug, she developed a maculopapular eruption on the face which, in a short time, extended to the trunk and extremities. Her medical history was negative, but there was a history of seasonal allergy in her mother. Twelve days later, she was admitted to hospital with fever, nausea and vomiting, generalized cutaneous eruption, and buccal mucositis. On examination, her vital data revealed a respiratory rate of 27/min, pulse rate of 110/min, and temperature of 39 °C. Her body weight was 12 kg. Her skin showed an erythematous eruption with target-like iris lesions on the extensor surfaces of the extremities. There were no lesions in her eyes or on her genitalia. No lymphadenopathy and organomegaly were detected. Respiratory and cardiac auscultation was normal.

Laboratory evaluation found a leukocyte count of $8.3 \times 10^9/L$, with 36% neutrophils and 64% lymphocytes. ESR was 20 mm/h.

Urinalysis and serum chemistry (fasting blood glucose, Na, K, BUN, creatinine, liver function tests) were normal, except for slightly elevated liver function test results: AST was 56 U/L and ALT was 77 U/L. A diagnosis of phenobarbital-induced EM was made and phenobarbital was discontinued. She was managed and treated. During admission, the patient showed cyanosis of the extremities without respiratory involvement, which was treated with nasal oxygen, 3–4 L/min. One week after admission, her symptoms resolved and she was discharged home.

Case 7

A 9-year-old girl was admitted to hospital with a history of headache, fever, and chill. With a diagnosis of epidural empyema, the brain abscess was evacuated. After evacuation, phenytoin, 100 mg three times daily, was started. Three weeks after starting the drug, an eruption developed on the face and progressively extended to the trunk, back, and extremities. Her medical and family histories were noncontributory. She gave no history of the recent use of any medications and had no previously known food or drug allergies. On admission, the patient was unwell. She was febrile with a temperature of 38.9 °C; she was hemodynamically stable. She had nausea and vomiting. On examination, the skin was erythematous with large bullae that progressively ruptured. There were no genital, mucosal, or conjunctival erosions. No lymphadenopathy and organomegaly were detected. Other examinations were normal. Blood tests and chest X-ray were normal. Liver function tests were normal. Serum albumin started to decrease and dropped to 1.8 mg/dL (NR, 3.5–5.2 mg/dL), and total protein was 4.16 mg/dL (NR, 6.6–8.8 mg/dL). A diagnosis of SJS/TEN was made, phenytoin was changed to valproate-Na, 5 cm³/day, and supportive treatment was initiated. Her eruption continued to spread and her bullae continued to



Figure 6 Ruptured bullae in a 9-year-old girl with Stevens-Johnson syndrome/toxic epidermal necrolysis

rupture (Fig. 6). Bathing daily with normal saline, and topical antimicrobials and lubricants were used. Amp dexamethasone, 8 mg three times daily, was started. After 3 days, the anticonvulsant therapy was discontinued. The eruption progressively disappeared, her condition improved, and she was discharged after 20 days when the skin had healed with extensive postinflammatory hyperpigmentation.

Treatment

The treatment of patients was started with immediate withdrawal of the potential causative drugs (barbiturates). To reduce the risk of infection, mortality rate, and length of hospitalization, the patients were barrier nursed in isolated rooms.

Intravenous fluid replacement was initiated in these cases and regular recordings of blood pressure and urine output guided fluid replacement. IVIG therapy, 0.5–2 g/kg (single dose or daily for 1–3 days), and systemic corticosteroid were administered. Analgesics were used for pain. Wounds were bathed with normal saline and sloughing tissue was gently debrided at every bathing to reduce the rate of infection, protect the unhealed areas, and reduce pain. The topical antimicrobial nystatin oral suspension was used on the ruptured blisters and after signs of healing. The ophthalmology service was consulted, various topical antimicrobials were given, and the eyes were washed frequently with normal saline. The patients with hypoalbuminemia received albumin, 1–2 g/kg, and anemic patients received packed cell transfusion. Medical care and procedures continued until wound healing was complete.

Discussion

A major problem of drug therapy, and one that confronts primary care physicians on a daily basis, is the risk of adverse

drug reactions (ADRs), which are a major and important healthcare problem.¹² Among them, the incidence of severe ADR is approximately 7% in hospitalized patients.¹³

A variety of hypersensitivity responses are responsible for most cutaneous reactions to drugs. The term “hypersensitivity syndrome” refers to a specific severe idiosyncratic reaction. These reactions typically include skin eruption and fever, often with hepatitis, arthralgias, lymphadenopathy, or hematologic abnormalities.^{14,15}

In an Iranian study,¹⁶ adverse cutaneous drug reactions were found in 6.2% of hospitalized children in a department of infectious disease; reactions were severe in less than 5% of cases.

Severe adverse cutaneous reactions, including SJS and TEN, have long been associated with the use of aromatic anticonvulsant drugs.^{17,18} Anticonvulsant hypersensitivity syndrome (AHS) represents a potentially life-threatening reaction to a number of anticonvulsants, including phenytoin, carbamazepine, and phenobarbital. This syndrome is characterized by fever, generalized eruption, and lymphadenopathy, but may present with other systemic complications. The incidence of this syndrome is estimated to be between 1 : 1000 and 1 : 10,000 exposures; however, an isolated eruption to anticonvulsants may occur in as many as 3–20% of patients receiving the drugs.¹⁹ The onset of hypersensitivity syndrome occurs at a mean of 2 weeks from the onset of drug exposure. The pathophysiologic processes involved are complex and are not completely understood.^{8,20} Although the precise mechanism causing hypersensitivity syndrome remains to be determined, current research centers on three areas. First, it is thought that patients with hypersensitivity syndrome exhibit atypical metabolism of the offending drug, which leads to the increased production of reactive metabolites.²⁰ Second, hypersensitivity syndrome may be immunologically mediated (mediated by lymphocytotoxic reactions). Immunologic studies have demonstrated that the dermal cellular infiltrate consists mainly of CD4⁺ T lymphocytes, whereas a predominance of CD8⁺ T lymphocytes is found in the epidermis and in blister fluid. This pattern of CD8⁺ T lymphocytes acting as effector cells in an acute cell-mediated reaction against allogenic antigens is similar to that of skin graft rejection.¹⁵ Third, some investigators believe that a strong genetic susceptibility to hypersensitivity syndrome may exist.²⁰

The prototypical lesion of EM is a targetoid, dusky, erythematous patch, found predominantly on the extremities, although, as the name implies, many different morphologies may be observed. EM minor is attributable almost exclusively to herpetic or mycoplasma infection, whereas EM major, considered by some to be synonymous with SJS, involves the mucous membranes and is associated with drug exposure in approximately 50% of cases. In SJS, bullae form on an erythematous base and confluent areas of skin detachment may be present. In contrast with EM minor, initial lesions of

SJS tend to occur on the face and trunk, and are associated with a 'burning' sensation or pain, an ominous sign of an impending severe reaction. At least two mucosal sites are involved in SJS. TEN is the most severe form in this reaction spectrum, occurring when large areas of skin sloughing affect more than 30% of the total body surface area.¹⁹

The annual incidence of EM has been estimated to be between 0.01 and 1%.¹ The incidences of SJS and TEN have been estimated to be 0.4–1.2 and 1.2–6 per million person years, respectively.^{1,2} Although TEN is extremely rare, it is often fatal and is a medical emergency. Early recognition of the disease and prompt referral of patients to an appropriate treatment center reduce the risk of infection, length of hospitalization, and increase the survival rate.^{20,21} These conditions occur more often in females than in males (1.6 : 1), are even rarer in children, and most commonly are drug induced.^{9,20,22} Constitutional symptoms are more common with TEN, but both TEN and SJS may present with fever that precedes the mucocutaneous eruption by 1–3 days. The mucocutaneous findings of both SJS and TEN rapidly progress over hours to days.¹⁹ Because the pathogenic mechanisms are poorly defined and the evolution of hypersensitivity syndrome is often rapid, no effective and specific treatment for this syndrome exists.¹⁵

The American Burn Association recommends that these patients be treated in a burn center because of the similarities between burn injuries and hypersensitivity syndrome, especially TEN.²⁰ Intensive management of the patients after prompt cessation of the suspected offending drugs (anticonvulsants) includes fluid resuscitation, treatment for alterations in the integumentary system, control of infection and sepsis, pain management, nutritional therapy, psychosocial support and rehabilitative services, and optimization of the environment for rapid re-epithelialization.^{11,20} Corticosteroid use is highly debated. These drugs are a mainstay in some units, but other investigators consider systemic corticosteroids to provoke prolonged wound healing, an increased risk of infection, masking of early signs of sepsis, severe gastrointestinal bleeding, and increased mortality.

Ocular complications from TEN are reported in 27% of patients. Conjunctival involvement may result in synechiae, persistent photophobia, visual impairment, or complete blindness.¹⁹ Specific eye care for patients with ocular involvement is essential. Prevention of ocular sequelae requires daily examination by an ophthalmologist. Eye drops, physiologic saline, or antimicrobials, if needed, are instilled every 2 hours.²¹ Fortunately, none of our patients had corneal involvement, and so were treated without residual severe ocular complications. Oral hygiene can be difficult in patients with extensive oral erosions, but various topical drugs are available.³

During hospitalization, Case 1 experienced numerous complications, including septicemia, for which he received systemic antimicrobials. He developed anemia requiring packed

cell transfusion. He also showed hypoalbuminemia during admission, which was treated with albumin, 1 g/kg.

Lesions of the gastrointestinal and respiratory tract are not uncommon in these reactions.¹⁹ Gastrointestinal involvement ranges from mild elevations of liver transaminases to severe gastrointestinal ulcerations and sloughing of intestinal mucosa.²³ Cases 1, 6, and 7 showed gastrointestinal complications: in Case 1, there was a distended abdomen, nausea, and vomiting; Cases 6 and 7 showed nausea and vomiting. After evaluation, they were treated symptomatically. The administration of IVIG had a beneficial effect on the survival of patients.⁹ We therefore administered IVIG (2 g/kg) to four of our patients. The administration of systemic corticosteroids in the treatment of SJS and TEN in an attempt to suppress the inflammatory process is controversial.²³ Emotional and psychiatric support must not be forgotten.²¹

These strategies seem to be successful and safe because, despite the serious condition of our patients, they all responded well. All survived and none developed scarring, with only hyperpigmented areas remaining at 1 year of follow-up.

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