Case Report

Lyell's Syndrome and Antimalarials: A Case Report and Clinical Review

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Abstract

Toxic epidermal necrolysis (TEN) or Lyell's syndrome is a rare, however, life-threatening mucocutaneous disorder with an epidermal detachment of a total body surface area (TBSA) of >30%. It is triggered by an idiosyncratic immune-allergic reaction to a drug, with many possible drugs implicated. Treatment success relies on early diagnosis and withdrawal of suspected/causative drug(s) and supportive care. Clinical evidence for specific therapies is still sparse. It is described a case of Lyell syndrome by sulfonamides for chemoprophylaxis of malaria. The patient presented with an extensive, rapidly evolving skin detachment, which progressed, despite supportive therapy, involving about 80% of TBSA. This led us to initiate a course of immunoglobulin with good clinical response. The aim of this work is to provide a discussion of the case and simultaneously make a practical literature review of TEN.

Keywords: Immunoglobulin, Lyell syndrome, malaria, sulfonamides, toxic epidermal necrolysis

Introduction

Toxic epidermal necrolysis (TEN), also known as Lyell's syndrome, was first described by the Scottish dermatologist Lyell in 1956. It is a life-threatening mucocutaneous disorder characterized by epidermal detachment >30% of the patient's total body surface area (TBSA). TEN is thought to be triggered by an idiosyncratic immune-allergic reaction to a drug, with more than 220 drugs implicated as causative agents.[1-3]

Although a rare disease, with 0.4–1.4 cases/million/year, TEN's mortality rate ranges from 25% to 70%, depending on age, initial body surface area of epidermal detachment and comorbidities.[2-5]

Mucocutaneous, ocular, lung, and intestinal epidermal sloughing can also occur. Infectious sequelae with the loss of the protective epidermal layer increase patient's mortality. There is no antidote and no universal consensus on treatment strategy. Treatment success relies on early diagnosis, withdrawal of suspected/causative drug(s) and supportive care directed to keep hemodynamic stability, pain management, and wound care to prevent infection.

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We describe a case of TEN secondary to sulfonamides that was managed in our Burn Unit.

Case Report

A 48-year-old Portuguese man, Caucasian, professional diver, working and living in Angola, with no significant medical history apart from several malaria episodes.

Four days after completing a 3-day prophylactic medication scheme for paludisme (sulfadoxine 500 mg/pyrimethamine 25 mg – S-P), he presented a flu-like syndrome, aggravated with fever and a pruritic facial rash, that extended to the trunk [Figure 1 resumes the progression and presentation of disease]. He was started on amoxicillin plus clavulanic acid, metronidazole, dexamethasone, loratadine, and ibuprofen. In <24 h, developed a severe mucosal damage

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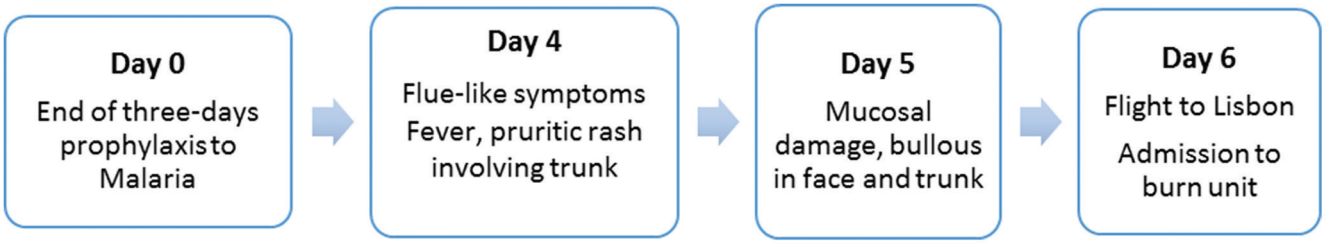

Figure 1: Clinical case presentation and evolution

with odynophagia and dysphagia, extensive bullous lesions on the face and trunk and a fever of 40°C. He was admitted to a medical clinic in Luanda, stopped all the previous medication, initiated fluid therapy and the day after decided to fly to Lisbon and directly to our hospital.

After evaluation by a multidisciplinary team (internal medicine and plastic surgery), a Lyell's syndrome was suspected, and he was admitted in our Burn Unit.

On skin examination, he presented a generalized exanthema with purpuric macules, bullae and erosions, with epidermal detachment – a positive Nikolsky sign [Figures 2-4]. Around 70% of TBSA was involved, including head, neck, anterior and posterior trunk, arms, and genitals. The oral mucosae had edema, erythema, and blistering. Ruptured blisters formed hemorrhagic erosions resulting in dysphagia and inability to speak. Ocular involvement, with mild erythema and mucous purulent exudate was present. Vital signs were stable with an elevated body temperature of 39°C, there were no significant changes in the cardiac and pulmonary physical examination. There were no abnormalities detected on chest X-ray and electrocardiogram studies.

Mortality scores, on admission were Simplified Acute Physiology Score II – 19; sequential organ failure assessment (SOFA) – 1. On admission, the severity-of-illness-score for TEN (SCORTEN),[5] was 2 (12.2% of mortality).

A skin biopsy, skin swabs, and blood culture were performed on admission. Femoral central venous catheter (CVC), radial arterial line, nasogastric tube, and urinary catheter were placed. The patient was monitored in the Burn Unit, started on fluids (Parkland formula), along with subcutaneous enoxaparin (40 mg/day); intravenous (IV) pantoprazole (40 mg/day) and morphine perfusion (0.05 mg/kg/h). Topical ophthalmic chloramphenicol and prednisolone every 8 h was instituted. He was followed-up daily by a plastic surgeon, an anesthesiologist, an ophthalmologist and a nurse team.

On the 3rd day after admission, there was a deterioration of the level of consciousness, persistent fever and progression of the cutaneous and mucosal lesions to a TBSA of 80%, becoming more hemorrhagic. SOFA and SCORTEN aggravated to 4 (58.3% of mortality), which led us to initiate a 3-day course of IV immunoglobulin (IVIG) (1 g/kg/day). On the 1st day of IVIG, he developed a mild to moderate side-effect reaction, that subsided with supportive therapy. After the 3rd day of immunoglobulin therapy, the skin lesions began to heal and clinical state improved progressively.

Since his admission, the patient was on spontaneous ventilation (FiO_2 40–60% adjusted to keep oxygen-hemoglobin saturation above 94%), despite severe mucosal lesions he maintained protective airway reflexes, no signs of respiratory compromise on chest X-ray or arterial blood gas analysis and good respiratory dynamic. Care to avoid pressure sores and to obtain an adequate temperature and humidity state was taken, daily aseptic dressings with paraffin gauze and iodopovidone and weekly sessions of balneotherapy for mechanical debridement of necrotic areas were done. These were performed under sedoanalgesia with midazolam, fentanyl, propofol and ketamine, maintaining spontaneous breathing. No biologic or synthetic skin substitutes were needed. Hemorrhagic lesions led to coagulopathy requiring topical hemostasis, blood transfusion, and occasional plasma therapy.

The skin biopsy evidenced epidermal necrosis with intense lymphocyte reaction and dermal-epidermal sloughing with preservation of the dermis, compatible with Lyell syndrome.

Infection control and periodic surface and blood cultures of the regions affected were drawn whenever indicated. Due to persistent fever, empiric antibiotic therapy with piperacillin and tazobactam plus gentamicin was initiated and later redirected to a methicillin-sensitive *Staphylococcus aureus*, identified in blood and CVC culture, to which he completed 7 days of flucloxacilin. It was also isolated, on his 15th day of admission, an *Escherichia coli* in genital lesions swabs, to which he completed 7 days of cefuroxime. All other blood cultures, skin swabs and urine cultures were sterile.

He presented progressive clinical improvement from the 5th day and epidermalization from the 10th day after admission at our Burn Unit. He was discharged to the plastic surgery ward on the 25th day. We verified total epidermalization of the affected areas, although with dyschromia and cutaneous hypersensibility with no residual mucosal or ophthalmic lesions [Figures 5-7].

Literature review

Background

TEN is a severe mucocutaneous exfoliative reaction. Stevens–Johnson syndrome (SJS) and TEN were considered

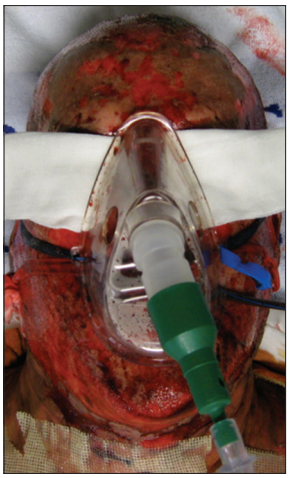

Figure 2: Face lesions before treatment (at admission)

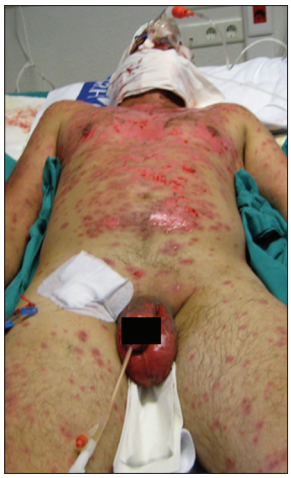

Figure 3: Thorax lesions before treatment (at admission)

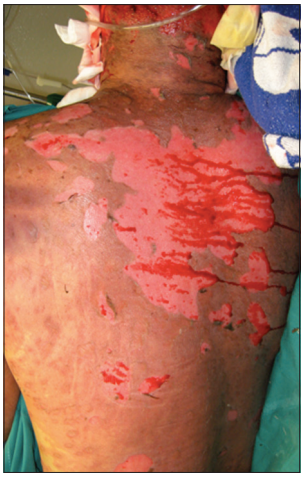

Figure 4: Torso lesions before treatment (at admission)

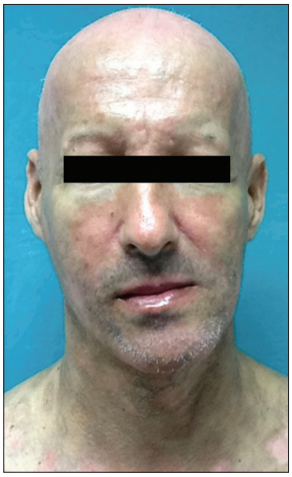

Figure 5: Face lesions at discharge (23rd day of burn unit)

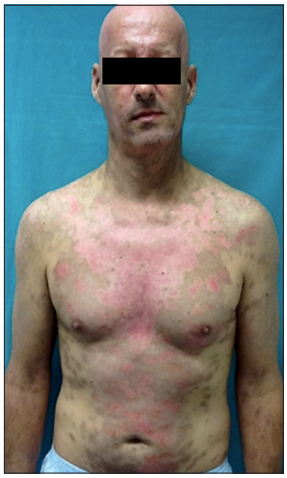

Figure 6: Thorax lesions at discharge (23rd day of burn unit)

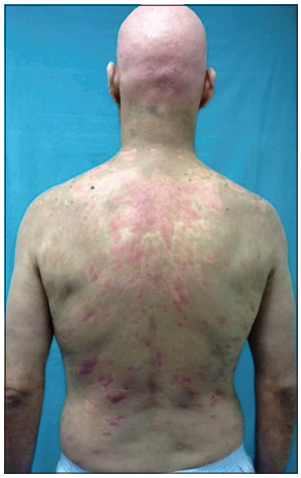

Figure 7: Torso lesions at discharge (23rd day of burn unit)

part of erythema multiforme (EM) spectrum of disease. EM has a less severe presentation with <10% TSBA involved, minimal mucous involvement and typical symmetrical target-lesions.[2,3,6] Nowadays, SJS and TEN (but not EM) are considered variants of the same pathologic process, differing only in the extent and severity of mucosal and/or cutaneous involvement.[3] According to Chan *et al*., TEN is presents with involvement of at least two mucous membranes, loss

of confluent sheets of epidermis exposing the dermis of at least 20% of TBSA, fever and a compatible skin biopsy (paucicelular infiltrates and widespread necrotic epidermis involving all layers).[7] In Europe, TEN is indiscriminately classified as being present when more than 30% or 10% of the TBSA is involved whether it presents with or without spots, respectively.[6] In the United States, SJS is defined as epidermal detachment >10% TBSA and TEN is defined as epidermal detachment >30% the TBSA while both SJS and TEN can have mucosal involvement. In between (TBSA 10–30%) there is overlapping of SJS and TEN.[2,3]

Etiology

In 90% of cases, TEN is triggered by an idiosyncratic immune-allergic reaction related to a drug.[2,3,8-12] More than 220 medications have been implicated, but only a few of them are most commonly involved [Table 1].[3,11,13] The incidence is higher in extremes of age, and there is a female/male ratio of 1.5:1.[3]

Recently, the EuroSCAR study estimated the risk of different drugs in SJS or TEN.[14] Covering more than 100 million inhabitants in hospitals of five European countries, this study confirmed the risk related to anti-infective sulfonamides, allopurinol, carbamazepine, phenobarbital, phenytoin, and oxicam-nonsteroidal anti-inflammatory drugs. Among newer drugs, strong associations were reported for nevirapine and lamotrigine, and weaker associations for sertraline, pantoprazole, and tramadol.

Plasmodium chloroquine-resistance increased TEN secondary to the association S-P, with a few fatal cases described in the literature.[15,16]

The possibility of TEN should always be taken into account when prescribing high-risk drugs.

Physiopathology

It is common understanding that this disease is the presentation of an unregulated immune reaction against epithelial cells; re-challenging an individual with the same drug can result in fast recurrence of SJS/TEN, pointing to an immunologic mechanism of sensitization and memory.[10,11,17,18]

Two pathogenic immune mechanisms are described: perforin-granzyme mediated cell apoptosis and Fas-FasL mediated cell apoptosis.[7] Drug intake leads to accumulation of toxic metabolites or immunoallergic mechanisms, with reactive metabolites behaving as highly immunogenic haptens. These trigger cytokines release (such as tumor necrosis factor [TNF]-α, interleukin [IL]-10 and IL-6), with CD95 receptor activation (Fas) leading to massive apoptosis of keratinocyte and mucosal epithelial cells.[3,8] The Fas-FasL pathway theory is based on a drug-mediated up-regulation, which triggers a downstream caspase cascade of apoptosis.[2-4,10] IVIG is thought to inhibit this reaction, but its effectiveness as a treatment modality remains debated.

Another accepted theory suggests that, in genetically predisposed individuals, drug metabolites accumulate in the epidermis and can induce an immunologic process similar to graft-versus-host disease.[8] On the other hand, several immune-histological studies and blister fluid analysis, point to T lymphocytes as the main character in the pathogenesis of SJS/TEN.[8,11,19]

How a drug, in a given patient, regulates the function of these key players leading to SJS/TEN, is still debated.

Diagnose

TEN usually develops 1–3 weeks after contact with a suspect drug with no consistent tests to conclusively prove the link.[3,5,10]

TEN is preceded by a prodromal phase (48–72 h) of a flu-like syndrome (fever, dysphagia, cough, gastrointestinal symptoms, myalgia).[3,10,20] Later this can progress, although inconsistently, to systemic symptoms with low albumin, leukopenia, anemia and possibly disseminated intravascular coagulation (DIC).

Mucosal and cutaneous lesions are characteristic. Mucosal lesions may be the first to appear, mainly involving the stratified squamous epithelium. Erosion and shedding of conjunctiva, respiratory, oral, pharyngeal, esophagus, urethral, anal, vaginal, and perineal mucosa can be found. However, oral, pharyngeal, conjunctiva and urethral surfaces are most frequently affected.[20-21] Cutaneous lesions predominate in sun-exposed areas and usually begin symmetrically on the trunk. The scalp, legs, and the distal part of the arms (except

Table 1: Causes of Lyell Syndrome

Antimicrobial	Anticonvulsants	Others	Nonpharmacological
Sulfonamides*[a]	Phenytoin*[b]	Allopurinol	Graft versus host disease (allogenic bone marrow transplantation)
B-lactams' (ampicillin, amoxicillin)	Carbamazepine	NSAIDS	Exposure to industrial chemicals and fumigants
Tetracycline's	Phenobarbital	Anti-retroviral	*Mycoplasma pneumoniae* infection
Quinolones (ciprofloxacin)	Valproic acid	Vaccines (smallpox, measles, diphtheria- pertussis- tetanus, poliomyelitis, influenza, BCG)	Genetic predisposition (HLA-B*5801 and HLA-B*1502)
Tuberculostatics		Corticoids	
Antifungal			

Adapted.[3,11,13] *[a]Most frequent etiology in adults, *[b]Most frequent etiology in children. NSAIDS: Nonsteroid anti-inflammatory, BCG: *Bacillus* Calmette–Guérin

palms and soles) are relatively spared. These lesions start as an acute macular erythematous rash with central blistering and target lesions with a dark red center and lighter red halo. Rapidly, they exhibit Nikolsky's sign (epidermal detachment by gentle lateral pressure on the skin). This detachment can become very extensive with a total epidermal loss in 24 h in severe cases. Diagnosis of TEN is largely clinical but has to be confirmed by skin biopsy histology.[3] Histological studies reveal widespread necrotic epidermis involving all layers. To rule out autoimmune blistering diseases, direct immune fluorescence staining should be performed, and no immunoglobulin or complement deposition should be detected.[10]

Re-epithelialization is evident in 1–3 weeks, although fever may persist without culture proven infection.

Other pathologies to include in the differential diagnosis of TEN are EM, impetigo, SJS, staphylococcal scalded skin syndrome, lupus erythematosus, pemphigus vulgaris, linear IgA dermatosis, bullous pemphigoid, cutaneous T-cell lymphoma, toxic shock syndrome, Kawasaki disease, graft versus host disease, and thermal or chemical burns.[1,10,20]

Only necrotic skin or detachable skin (Nikolsky +) should be included to evaluate the TBSA involved. The extension of involvement is a major prognostic factor.[20]

Treatment

No randomized controlled trials or guidelines exist for TEN's treatment. Guidelines proposed by Avakian *et al.* in 1991 and revised in 2007 by Fromowitz *et al.* can be considered a starting point.[22,23] These are built on a multidisciplinary approach, early diagnosis, withdrawal of suspected/causative drug(s), supportive care and definite therapies with three primary goals: hemodynamic stability, pain management, and infection control.

The SCORTEN is now the most commonly used scoring system. Apart from evaluating the severity of the clinical picture, can aid in decision making. A score of 3 or more should be treated in an Intensive Care Unit if possible.[10]

Isolation, appropriate wound management, constant nurse control and the availability of technologically advanced devices, make the Burn Unit the most suitable place for the treatment of TEN patients according to several authors.[3,10,20,24]

Garcia-Doval *et al*. have shown that early culprit drug withdrawal and the shorter the half-life of the drug, the better the prognosis.[24] After discontinuing unnecessary and suspect medications, first-line management is fluid and electrolyte replacement, acid-base, metabolic regulation and topical skin management. Fluid replacement should be started with crystalloids. The amount to be administered is controversial. Most authors use Parkland's formula and administrate Ringer's solution, as in burn patients.[3] Others state that third space loss phenomenon and changes in vascular permeability are absent, contrary to burn patients, with less need for fluid-aggressive therapy.[24,25]

TEN patients present several nutrition management difficulties. Oropharyngeal lesions may cause difficulties in eating, drinking and enteral tube placement. High nutritional requirements due to an hypermetabolic response, appear to be related to TBSA affected.[3,25] Nutrient absorption can be altered by gastrointestinal mucosa involvement. Some authors suggest avoiding nasogastric tube because of gastrointestinal mucosae potential involvement;[26,27] however, this might be the only feeding alternative. Total parenteral nutrition should be started in patients without an enteral route.

As for other critically ill patients, analgesia, prophylaxis for deep vein thrombosis and erosive gastric ulcer, daily physical therapy, prevention of pressure sores, and infections cannot be overemphasized.[3,20]

Periodic laboratory analysis and cultures, according to clinical context, should be collected. This is also valid for X-ray and gasometrical analysis to evaluate respiratory compromise.

Antibiotic therapy should be guided by high suspicion of infection, microbiological cultures, and antibiogram,[28] except when there is leukopenia.[20] Invasive procedures should be reduced to a minimum and avoid affected areas.

Topical treatment

Topical wound care is essential in the treatment of TEN. The ideal wound dressing for re-epithelialization should preserve physiologic conditions, protecting the wound and allowing unrestricted movements. It must also be permeable, easy to apply, nontoxic, nonadherent, and low priced.

Some authors suggest aggressive operative debridement, while others support a conservative approach since blistered skin acts as a natural biological dressing, which likely favors re-epithelialization.[3] Whichever approach is chosen; the exposed dermis should be protected with some form of coverage.

Detached epidermis should be removed under sedoanalgesia,[10,28] avoiding general anesthesia and endotracheal intubation. When the dermis is intact, nonadhesive wound dressings are enough, assuring aseptic conditions and daily dressings.[29]

Exposed areas should be sterilized using chlorhexidine or silver nitrate 0.5%,[26,30] and covered with paraffin gauze, biological materials, synthetic skin substitutes, or adsorbent skin dressings.[3,10,20,26]

Aquacel Ag™ was recently reported in TEN wound treatment, does not need daily changing and can remain in place for 3 days or until epithelialization is complete. According to some authors, it is cost effective, reduces wound infection, the frequency of dressing changes and pain levels.[3]

The use of sulfonamide-containing solutions is contraindicated due the possible implication in the pathophysiology of the syndrome and additionally, might delay re-epithelialization.[3,23]

Pharmacological treatments

The role of the immune system in TEN's pathophysiology inspired the administration of various agents with immunologic actions. Some institutions use systemic corticosteroids, immunosuppressives (cyclophosphamide, cyclosporine), anti-TNF-α agents, plasmapheresis, and human IVIG. Nevertheless, there is no consensus on treatment effects. Prompt withdrawal of the suspected drug is the first-line therapy[10,20] and was, for many years, the only validated one to reduce mortality.

Despite some success, corticosteroids and immunosuppressives are not considered as a standard treatment for TEN.[31] Some authors consider there are risks of administering an immunosuppressant drug to an already immunosuppressed individual.[20]

Plasmapheresis is reported to lead to some success.[3] Nevertheless, there is no agreement about the efficacy of this expensive treatment, its benefits are still unclear and there are series of nonresponding patients.[2,32]

N-acetylcysteine anti-oxidant effects, in high doses, might inhibit cytokines production and release, like TNF-α and IL-1, involved in TEN's physiopathology.[33]

IVIG is the most recent therapeutic approach to TEN, 24 proposed in 1998 by Viard *et al*.[32] It's pharmacokinetics is based on blockage of CD95 cell-surface receptor (Fas) that induces keratinocyte apoptosis.[34] IVIGs are obtained from plasma of blood donors, fractionated and purified until obtaining predominantly IgG (90–98%), traces of IgA, IgM, CD4, CD8, human leukocyte antigen molecules, and cytokines. IVIG dosage, however, is still unclear. Viard *et al*. indicated a protocol in which IVIG should be infused at doses of 0.7 g/kg daily for 4 days (total dose 2.8 g/kg) and with methylprednisolone 250 mg/6 h for the first 48 h.[34] This protocol was modified successively by different authors.[5,8,34-37] Despite the potential biases and although they are not directly comparable, most studies suggested a benefit, of high-dose IVIG, in TEN's mortality.[34-37]

Trent *et al*. conducted a systematic review from 1992 to 2006, to study the dose-response relationship. Despite the study limitations stated by the authors, results showed that within each 1 g/kg increase in IVIG dose, there was a statistically significant 4.2-fold increase in TEN patient survival.[37]

IVIG treatment is still not globally accepted. In Portugal, there are few cases in the literature and none comparing IVIG with other conservative therapies.

Complications and long-term sequelae

About 40% of survivors of TEN have residual and potentially disabling lesions.[3] After the acute period, skin and mucosal sequelae are unfortunately frequent with a threat to life or its quality.

Sepsis is responsible for more than 50% of mortality, especially if it is associated with DIC. Common pathogens in TEN sepsis are *S. aureus* and *Pseudomonas aeruginosa*.[20-22]

Ocular involvement can lead to eyelid fusion, corneal ulcers, and subsequent blindness. Pulmonary sequelae range from chronic bronchitis, bronchiectasis, obliterans bronchiolitis, pneumonia or acute respiratory distress syndrome. These may dictate the need to invasive mechanical ventilation, which can be challenging in these patients. There might also be a reduction in diffusing capacity of the lung for carbon monoxide (DLCO) of 35–40% even in those who do not require mechanical ventilation.[38]

Other sequelae as dysphagia, diarrhea, esophagic stenosis or rupture, hepatitis, vaginal and ureteral stenosis, hair loss, nails dystrophy, hypo or hyperpigmentation can also be seen.[3,10]

Prognosis

There are several clinical and laboratory factors that influence adversely the prognosis. The TBSA involved, advanced age, significant comorbidities, delay in suspending the culprit drug, concomitant intake of multiple drugs, need for multiples transfusions and a long re-epithelialization time (more than 9 days). Neutropenia is the most consistent laboratory data to prognosis. Another important factor is more than 48 h delay in admission to an Intensive Care/Burn Unit.[20]

Discussion

Despite rare, TEN's is a potentially life-threatening disease. Sulfonamides, one of the main culprit drugs, are increasingly used to replace chloroquine due to the emergence of resistances. Furthermore, sulfonamides are used in the treatment and prevention of opportunistic infections in AIDS patients. Accordingly, it is expected that TEN's incidence will increase.

This clinical case report was a severe case with an extensive area involved with several negative prognostic factors present. The implicated drug and clinical picture were not promptly recognized, and the patient was exposed to various possibly implicated drugs further confusing the diagnosis and delaying the most effective measure – culprit drug withdraw. However, the order of events suggests that the disease was secondary to anti-*Plasmodium* prophylaxis with S-P. The initial clinical picture could be easily confused with a common flu or an allergic reaction (development of skin rash by day 5) which may have contributed to a delay in clinical recognition, admission to a Burn Unit and the beginning of treatment. This delay, in turn, might have hastened the progression of the disease, with an extremely high TBSA compromised. This appeal's for clinician's attention, since a high degree of suspicion and a simple early attitude, can have a significant impact on mortality and morbidity.

Furthermore, we should notice that unrecognition of disease severity and undertreatment in Luanda allowed worsening of symptoms, which motivated the patient to get discharge and

travel alone to Lisbon - a significant risk for the patient and others since the diagnosis was unclear.

At arrival, the hemorrhagic cutaneous lesions quickly led to the need of transfusion and progressed despite support therapy, until treatment with immunoglobulin was initiated.

An important mucosal surface involved is the respiratory tract with bronchial epithelium sloughing and hypoxemia in up to 30% of cases and need for invasive ventilatory support.[3] The decision to intubate the patient was deferred at admission since there was no airway compromise. The need for intubation was reevaluated daily and postponed since the patient maintained airway reflexes and no respiratory compromise. There was no need for support apart from pulmonary rehabilitation. Ophthalmologist consultation early at arrival with treatment and daily follow-up is important and might have been fundamental to avoid sequelae.

We want to point out that fever does not mean infection and we probably should have been less aggressive in this regard. The patient's initial cultures were negative, and the persistent fever was probably part of the inflammatory response rather than infection-associated. However, the severity of the disease led us to adopt a more careful and preventive attitude and initiate empiric antibiotics.

Despite the clinical picture severity, he was a diver with a very good physical condition, which may explain the minor laboratory, respiratory and infectious repercussions, as well as, the fast recovery with few short-term sequelae. The patient already presented with some hair loss and hypopigmentation. As for long-term sequelae, he must be followed-up closely. Despite no need for mechanical ventilation and minor respiratory compromise, a reduction in DLCO, as well as, different degrees of fibrosis and obstructive sequelae, like chronic bronchitis and bronchiolitis obliterans, can develop. Gastrointestinal and ureteral sequelae such as stenosis can also be seen.

As for treatment, no definite therapy, other than meticulous cutaneous management, and general conservative measures has been proven effective. Corticosteroids, immunosuppressants, N-acetylcysteine, plasmapheresis and IVIG, although still enclosed in controversy, seem to contribute to a reduction in mortality and morbidity.[31,33,37]

In our opinion, despite the lack of randomized controlled trials, early administration of immunoglobulin should be considered alongside supportive care for the treatment of TEN, given the absence of other validated specific therapeutic alternatives.

The clinical improvement in this case led the example of good outcomes with the use of immunoglobulin, which was included in the treatment armamentarium of our Burn Unit and as part of a multidisciplinary treatment protocol that is being developed.

Conclusion

We presented a patient with TEN secondary to anti-malarial treatment with S-P. Despite rare, it is very likely that the incidence of this syndrome will increase. Sulfonamides, one of the main culprit drugs, are increasingly used to replace chloroquine due to the emergence of resistances. They are also used in the treatment and prevention of opportunistic infections in Acquired Immune Deficiency Syndrome patients.

TEN is more than an acute skin failure. All organs can be involved leading to a potentially life-threatening process with a high mortality rate (25–70%). Clinical recognition and early withdrawal of the offending agent are essential. There is no specific therapy other than meticulous cutaneous management, and general conservative measures. Our experience with IVIG is still sparse, nevertheless positive, and will encourage future research in our unit.

Specialized critical care units should follow a treatment plan or protocol to standardize clinical care. However, there should be an opportunity for improvement and individualization.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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