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REVIEW

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Severe cutaneous adverse reactions: emergency approach to non-burn epidermolytic syndromes

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Abstract *Introduction:* Although severe cutaneous adverse reactions (SCARs), such as Stevens–Johnson syndrome and toxic epidermal necrolysis, are rare, they are associated with considerable morbidity and mortality. *Methods:* The current knowledge regarding background, differential diagnoses, critical care and implications for inter-hospital emergency medical service (EMS) transport of these patients is discussed. *Conclusion:* SCAR patients will substantially benefit from early interdisciplinary care and thorough consideration of complications during EMS transport and intensive care treatment.

Keywords Toxic epidermal necrolysis · Stevens–Johnson syndrome · Critical care · Emergency medical service · Patient transfer · Burn center

Introduction

Severe cutaneous adverse reactions (SCARs) are unpredictable and rare. Nonetheless, they are known to be associated with high morbidity and mortality. Adverse drug reactions, altered immune response and viral or bacterial infections are the primary triggers of these syndromes. Patients require admission to specialized centers, usually burn trauma centers, which are embedded in a critical care infrastructure and offer appropriate treatment of large cutaneous defects [1]. Direct admission to these centers is unusual; most patients are first admitted to regional medical or dermatological departments. Depending on the catchment area of the burn trauma center, inter-hospital transport is provided by either ground ambulance or helicopter.

The attending emergency medical service (EMS) team should be aware of the complex pathophysiology of these patients. Guidelines and literature regarding inter-hospital transport of patients who present with severe epidermolytic syndromes are not published. This article provides a short, systematic review of the background, critical care and complications of SCARs, with considerations for the EMS transport phase.

Definitions, clinical presentation and differential diagnoses

Clinical classification of non-infective SCARs distinguishes three conditions that present with extensive epidermolysis [2].

1. Stevens–Johnson syndrome (SJS)
2. Stevens–Johnson syndrome/toxic epidermal necrolysis (SJS/TEN)-overlap
3. Toxic epidermal necrolysis (TEN)

These reactions are considered a single disease entity with different levels of severity. They are associated with cutaneous erythema, progressive blistering, epidermolysis and mucosal erosions. Primary clinical manifestations are fever and malaise, followed by cutaneous blisters and erosive mucosal lesions of the mouth, lips, eyes and genital area. Cutaneous lesions often occur several days prior to mucosal erosions, but this order may be reversed.

The cutaneous eruption of SCAR is characterized by generalized and advanced epidermolysis with mobility of the affected epidermis upon healthy skin and epidermal detachment on the slightest friction, known as Nikolsky phenomenon (Fig. 1) [3]. Distinguishing between the different stages of skin detachment, especially in the acute phase, may be difficult, even for dermatologists. Due to the dynamic course of epidermolysis, different stages have been defined to classify these reactions. Classification is based on the calculation of skin detachment related to the total body surface area (TBSA) and the macroscopic signs of cutaneous involvement (Table 1). Epidermolysis under 10% TBSA is defined as SJS, whereas detachment of 10–30% TBSA is classified as SJS/TEN-overlap (Fig. 2). The condition with the most extensive form of cutaneous involvement is TEN, with epidermolysis similar to second-degree burns (greater than 30% TBSA). The lesions found in these reactions are so-called targets that are differentiated into three types. The typical targets are round nummular lesions of three concentric zones. Atypical targets are less well defined and are either flat with a central blister or raised due to infiltration of inflammatory cells. Macules and flat, atypical targets may become confluent as the blisters develop upon them. Stevens–Johnson syndrome, SJS/TEN-overlap and TEN are characterized by the presence of macules and flat atypical targets (Fig. 3). A second, but very rare form of TEN presents without macules or targets, but rather with large areas of erythema. One additional syndrome, erythema (exudativum) multiforme majus [E(E)MM], has a cutaneous involvement of less than 10% TBSA that usually does not require intensive care and presents with typical or raised targets with similar histological features [2, 4].

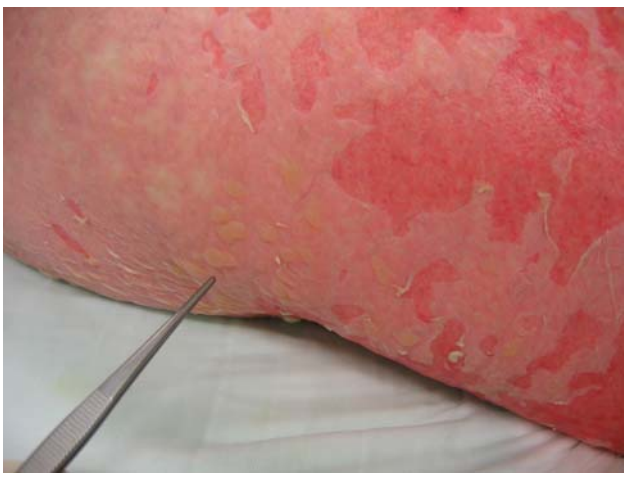

Fig. 1 Generalized and advanced epidermolysis with mobility of affected epidermis upon healthy skin and epidermal detachment on the slightest friction is known as Nikolsky phenomenon

Histological diagnosis by skin biopsy is the only reliable method to confirm the kind of cutaneous reaction, although histology must be considered in relation to the macroscopic clinical picture. In cases of SJS, SJS/TEN-overlap and TEN, histology reveals a subepidermal separation, and dermal infiltrates are located superficially and perivascularly. Eosinophils are frequently observed in E(E)MM and SJS, but are less common in patients with the most severe forms of TEN [2, 5].

Formerly, TEN was classified together with staphylococcal scalded skin syndrome (SSSS) by the term "Lyell's syndrome" [6]. A severe epidermolytic syndrome with an infectious background, SSSS is the main differential diagnosis of TEN. It results from colonization or infection with a strain of *Staphylococcus* species that produces epidermolytic toxins. Those toxins may be identified by staphylococcal lysotyping. The severity of SSSS ranges from insignificant focal skin blistering to extensive, life-threatening exfoliation. Although SSSS presents with similar clinical symptoms to TEN, target lesions are not observed, and mucosal erosions are rare. Histology shows subcorneal epidermal splitting without epidermal necrosis or inflammatory cells in the corium. Unlike SJS, SJS/TEN-overlap and TEN that present as a disseminated confluent exanthem, SSSS is characterized by widespread erythema [7].

Other differential diagnoses of SCAR with a background of bacterial infections are necrotizing fasciitis and purpura fulminans, both of which cause considerable morbidity and require early and aggressive antibacterial and surgical therapy.

Autoimmune blistering skin diseases, such as Pemphigus vulgaris or Bullous pemphigoid and generalized bullous fixed drug eruption (GBFDE), are non-infectious differential diagnoses [8, 9].

Epidemiology

The incidence of SJS, SJS/TEN-overlap and TEN is approximately one to two cases per 1 million inhabitants per year, whereas SSSS appears less frequently, with approximately one case per 10 million inhabitants per year [9–11]. Reported mortality rates for TEN vary

Table 1 Classification of the consensus definition (Bastuji-Garin et al. 1993 [2])

Criteria	EM majus	SJS	SJS/TEN-overlap	TEN with maculae	TEN on large erythema
Skin detachment(% of TBSA)	<10%	<10%	10–30%	>30%	>10%
Typical target lesions	+	−	−	−	−
Atypical target lesions	Raised	Flat	Flat	Flat	−
Macules	−	+	+	+	−
Distribution	Mainly limbs	Wide-spread	Wide-spread	Wide-spread	Wide-spread

EM Erythema multiforme; *SJS* Stevens-Johnson syndrome; *TEN* toxic epidermal necrolysis; TBSA, total body surface area

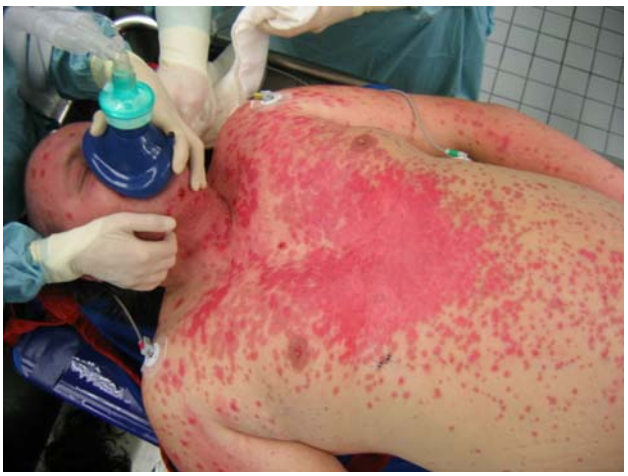

Fig. 2 Admission of a male patient presenting with Stevens–Johnson syndrome/toxic epidermal necrolysis overlap (epidermal detachment of 10–30% total body surface area)

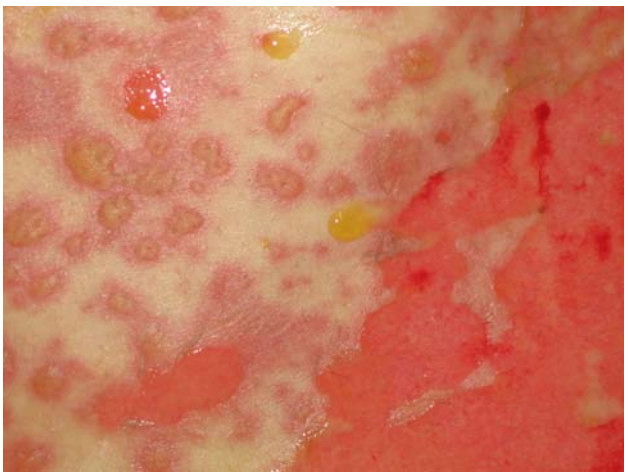

Fig. 3 The fluid composition of toxic epidermal necrolysis blisters may have a three-fold increase in albumin and protein compared to burn blisters

widely, from 20 to 80%. In a German population-based study, SJS had a mortality rate of less than 10%, SJS/TEN-overlap had a mortality rate of approximately 25%, and that of TEN was about 45% [9].

Table 2 Independent predictor variables of TEN (SCORTEN) (Bastuji-Garin et al. 2000 [12])

Age (≥40 years)
Heart rate (≥120/min)
Malignity
Initial epidermolysis (≥10% TBSA)
Serum urea (≥10 mmol/l)
Serum bicarbonate (≤20 mmol/l)
Serum glucose (≥14 mmol/l)

TEN Toxic epidermal necrolysis; *TBSA* total body surface area

The predictive variables for mortality in TEN have been summarized (SCORTEN) by evaluating epidemiologic and diagnostic parameters at certain intervals (Table 2). The identified risk factors are age above 40 years, malignancy, tachycardia above 120 beats/min, an initial percentage of epidermal detachment above 10%, serum urea above 10 mmol/l, serum glucose above 14 mmol/l and bicarbonate below 20 mmol/l [12].

Underlying cardiovascular and metabolic diseases, bleeding complications and sepsis often result in fatal multiple organ failure [13]. In recent studies, outcome prediction was more precise if the patient's status was analyzed more frequently and when the enlargement of cutaneous defects, respiratory involvement and age were better considered [14–16].

SSSS is associated with a mortality rate of 4% in infants and possibly greater than 60% in adults. There are two incidence peaks in this rare syndrome. The first and most likely occurrence is in infants and young toddlers, and the second is in adults with relevant co-morbidities [7, 11, 17].

Etiology and pathogenesis

Certain medications, an altered immune response and a genetic susceptibility are predisposing factors to the development of SCARs. The EuroSCAR study, a multinational case-control study covering more than 100 million individuals, evaluated the risk of medications to induce SCARs [18]. Whereas the risk of some well-known, high-risk drugs [allopurinol, anti-infective sulfonamides, several antiepileptic agents and non-steroidal

anti-inflammatory drugs (NSAIDs) of the oxicam-type] could be confirmed, a high relative risk was estimated for some new substances (lamotrigine, nevapirine). The incidence of SJS and TEN associated with allopurinol appears to have increased recently, a phenomenon that possibly represents a growing population using the drug or taking a higher dose [19]. In the pediatric population, the use of acetaminophen (paracetamol) was identified to increase the risk for developing SCARs. This was in addition to drugs that were already known to be highly suspect [20].

An immediate reaction to a medication is rare. The typical latency between starting a medication and the onset of an adverse reaction is 4–28 days and is rarely more than 8 weeks [18–21]. The primary agents triggering SCARs are summarized in Table 3.

The detailed mechanism of severe epidermolytic syndromes is still unknown. Here, we discuss immunological modulations as well as different forms of drug metabolism. Keratinocytes appear to play a major role in the pathogenic mechanism. Biochemical and morphological studies performed on early epidermal lesions demonstrated that keratinocytes undergo apoptosis, which is mediated by the Fas–FasL interaction or through cytotoxic T-cell release of perforin and granzyme B. Increased serum levels of soluble FasL (sFasL) have been reported in some TEN patients, supporting these findings [22–24]. Recently, it has been demonstrated, that the amount of granulysin in the blister fluid of SCAR patients is strongly related to the severity of the disease [21].

The genetic associations between human leukocyte antigen (HLA) alleles and the susceptibility to develop SJS or TEN are drug-, phenotype- and ethnicity-specific [25, 26]. Individual assessment of genetic predisposition before exposure to high-risk substances may be a future option for patients. Additional knowledge is needed in order to develop clinically relevant diagnostic methods in this field.

Table 3 Medications associated with high risks of SJS or TEN (Mockenhaupt et al. 2008 [18])

Nevirapine
Lamotrigine
Carbamazepine
Phenytoin
Phenobarbital
Cotrimoxazole and other anti-infective sulfonamides
Sulfasalazine
Allopurinol
Oxicam-NSAIDs

SJS Stevens–Johnson syndrome; *TEN* toxic epidermal necrolysis; *NSAID* non-steroidal anti-inflammatory drug

Table 4 Implications for emergency approach and EMS transport of SCAR patients

Discontinuation of inducing medication (if not already performed)
No administration of steroids and no prophylactic medication (e.g., antibiotics) until differential diagnosis is confirmed
Cardiovascular support (continuous fluid administration using crystalloids, prevention of volume overload, appropriate vasopressive and inotropic therapy)
Sufficient oxygen supplementation (by mask whenever possible, no prophylactic tracheal intubation)
Analgesia and anxiolysis (e.g., sub-dissociative ketamine, benzodiazepines, low-dose opioids)
Prevention of hypothermia (cabin conditioning, rewarming devices, blankets)
Anti-adhesive and antiseptic wound dressing
Expectation of severe mucosal bleedings (prepared oro- and naso-pharyngeal tamponades, prepared suction unit)
Expectation of rapid decrease of general condition (prepared tracheal intubation devices)

EMS Emergency medical service; *SCAR* severe cutaneous adverse reaction

Clinical therapy and complications

The therapy for SCARs that most experts agree upon is supportive critical care and the limitation of complications. Standardized protocols and widely accepted therapy schemes, however, are lacking. Furthermore, the clinical approach does not clearly delineate differences between pediatric and adult care strategies [27].

Initiating care

Early hospitalization of patients suffering from a SCAR is of utmost importance. Patients with TEN may deteriorate rapidly after presenting the first clinical signs. Emergency departments should be aware of these rare, but often life-threatening, diagnoses. We recommend an early call for advice from a specialized center to initiate appropriate and timely intensive care (Table 4) [28, 29].

Resuscitation

A major goal of supportive care is resuscitation and cardiovascular stabilization to maintain sufficient mean arterial blood pressure (ABP; >65 mmHg), central venous pressure (CVP; 8–12 mmHg) and central venous oxygenation ($Svco_2$; >70%) for adequate tissue oxygenation and renal perfusion [30, 31]. The trend of CVP under ongoing therapy may be much more relevant than recommending isolated goal numbers to assess the hemodynamic situation and fluid demand [32]. Recent recommendations of the desired hemodynamics in critically ill children in the ICU setting are an $Scvo_2$ of >70% and a cardiac index of 3.3–6.0 l/min per m^2 [33]. The

urinary output should be kept above 0.5–1.0 ml/kg per h (1.0–2.0 ml/kg per h in infants), but it should be recognized that TEN patients develop less extensive fluid loss and edema compared to burn patients [34]. Over-aggressive fluid resuscitation may be associated with severe intestinal edema, possibly resulting in intraabdominal hypertension and abdominal compartment syndrome. Intraabdominal pressure should be monitored using frequent measurement of bladder pressure [35, 36].

Patients with an adverse cardiovascular history may be more at risk of volume overload and the above complications. Prodromes of severe destabilization of gas exchange and circulation may be pulmonary edema, cutaneous edema and intestinal edema. The lack of intravascular fluid with simultaneous signs of overload characterizes this critical stage. Continuous invasive hemodynamic monitoring, therefore, should control fluid resuscitation and catecholamine therapy. Despite invasive monitoring, overadministration of fluids may be measured and recognized with certain latencies, due to the complex mechanisms of intracorporal fluid distribution/shift through vascular and interstitial compartments. Confirmed volume overload should be reversed by paracentesis or hemodialysis [37]. Frequent echocardiography and chest radiography are useful tools to monitor cardiac pump function and to identify pulmonary hypertension. Subsequent inotropic and vasodilator therapy may bridge the gap between the supply and demand of fluid administration [33, 38].

All intravenous and arterial lines should be sutured in place without taping or covering in order to avoid further skin damage.

Supportive care

The patient should be placed in a positive pressure isolation unit until a report of negative microbials (e.g., methicilline-resistant *Staphylococcus aureus* infection) is confirmed. Environmental temperature should be held greater than 30°C to avoid hypothermia and shivering (Fig. 4) [39]. Additional heat shields or lamps may be used during wound care procedures.

Frequent respiratory support and training exercises by physical and respiratory therapists should be performed as early as possible in order to prevent pneumonia and to maintain spontaneous breathing and respiratory competence when tracheal and pulmonary mucosa is affected.

Enteral nutrition should be maintained with a hypercaloric diet and monitored by calorimetry rather than fixed or calculated nutrition schemes. Serum albumin should be kept within normal ranges and may require intravenous substitution, since the fluid composition of TEN blisters may have a three-fold increase in albumin and protein compared to burn blisters [39–44]. Frequent evaluation of the patient's enteral peristalsis may help identify paralysis, and advanced enteral stimulation should be initiated at an early stage. Defecation should be encouraged using pharmacological rather than mechanical measures in the acute phase to avoid the risk of enteric mucosal bleeding. Gastric ulcer prophylaxis by antacids has been shown to reduce the risk of gastric bleeding [45].

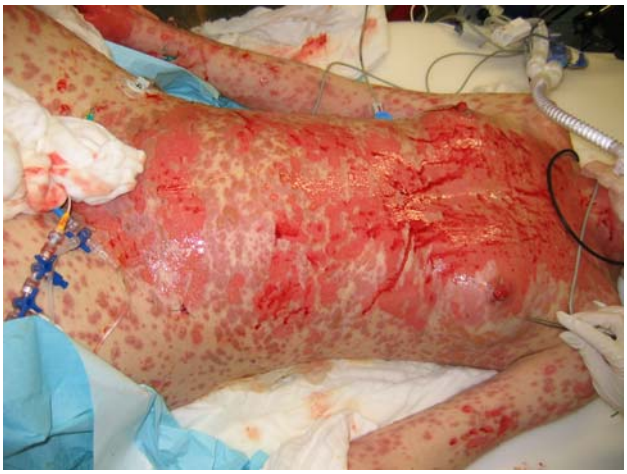

Fig. 4 Toxic epidermal necrolysis in a female patient covering more than 30% of the total body surface area. A special critical care infrastructure such as that provided in burn centers with positive pressure units providing a constant environmental temperature of more than 30°C and an adjustable atmospheric humidity of 70% should be considered in the early course of the disease

Bleeding complications, which could be possibly provoked by anticoagulation therapy, and the risk of thromboembolic complication due to immobilization present a therapeutic dilemma. In the acute phase of TEN, a no-touch strategy or at least very deliberate movement of the patient accompanied by anticoagulation therapy may decrease further cutaneous defects and thromboembolic complications [39, 46, 47].

Nosocomial infections may be avoided or at least decreased if strictly sterile nursing and physical examination are consistently performed. Frequent systemic and local microbial surveillance is crucial to antimicrobial therapy management. Liberal antibiotic prophylaxis should be avoided, as this may trigger and exacerbate epidermolytic syndromes and fungal infections [39, 48]. Cutaneous superinfections and catheter-related infections may lead to severe systemic bacterial and fungal infections, subsequent sepsis and multiple organ failure [1, 13]. All catheters should, therefore, undergo microbiological examination after removal.

Immunomodulating therapy

Steroid therapy for a SCAR remains a continuing controversy. The majority of studies have found that long-term steroid application is associated with cutaneous and systemic bacterial and fungal superinfections, masked

septic symptoms, a delayed presentation of epidermolysis and delayed re-epithelization, an increased length of hospital stay and increased mortality [49]. Other studies have found beneficial effects of short-term corticosteroid in the treatment of SJS and TEN [50]. These syndromes have also been observed in patients with long-term steroid use for other conditions [51]. The recently published EuroSCAR study did not conclude whether corticosteroids might be a direct cause of SJS and TEN, a risk factor as a result of modifying the immune response or a confounder [18]. Unlike SJS and TEN, the use of steroids is strongly contraindicated in differential diagnoses with infectious backgrounds, especially in SSSS.

A few studies regarding intravenous immunoglobulins (IVIG) in TEN therapy seemed promising, although sample sizes are small and subject to considerable bias. Unless randomized controlled trials are performed, there will not be enough evidence for a general recommendation of immunoglobulin therapy for SCARs [52–56]. The performance of multi-center approaches is very difficult because of the low incidence and the variety of individual courses. Further smaller and standardized trials may offer new perspectives on the treatment of patients suffering from SCARs.

Wound care

Due to the large wound surfaces, an initial therapy similar to that used for second-degree burns is the method of choice. Large, tight cutaneous blisters should be aspirated, and the sloughed epidermis should be removed. In contrast, smaller blisters with fixed surrounding skin may remain after the decompressive incision. If the detached skin is left in place to act as a biological dressing, wound healing may be improved, but it may also lead to an increasing risk of bacterial and fungal colonization that could possibly result in a systemic infection [13, 39, 48]. Based upon our experiences, this kind of antishear therapy may be an option under heightened microbial surveillance and lower TBSA skin detachment.

Generally, wounds should be dressed with liquid aseptic solutions (e.g., chlorhexidine, silver nitrate or octenidin) and covered with aseptic blankets (e.g., with a silver layer). Some authors have postulated that sulfonamide dressings should be avoided because of their potential to trigger severe adverse cutaneous reactions, whereas recent studies have not revealed evidence regarding the potential cross-reactivity of sulfonamides [39, 52].

Wound coverage with artificial material may be useful if wound progression is limited and the absence of local infection is confirmed. Biobrane® or nanocrystalline silver dressings, such as Acticoat® applications, have been reported in recent studies to improve outcomes in some patients, whereas other centers have reported successful treatment using conservative procedures (Fig. 5) [39, 57–59].

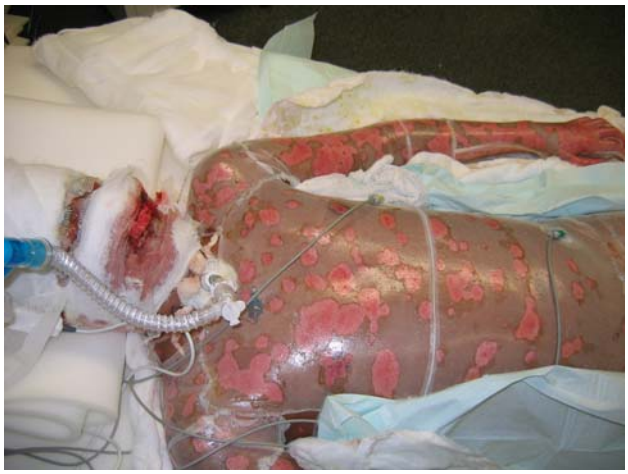

Fig. 5 Biobrane® coverage may be an alternative to conservative approaches if wound progression is limited and the absence of local infection is confirmed

Wound dressing changes and, if needed, cautious debridement of dead epidermis should be performed regularly. Operative debridement of deeper skin should be avoided, as this may cause further damage and consecutive healing complications that lead to scars. The wound healing process may be improved when the patient undergoes frequent bathing therapy during the re-epithelization process of the epidermis. Special fluidized airbeds are frequently used in the therapy of burns and large TBSA epidermolysis. Although they provide minimal shearing potential for the detached skin, they may cause thermoregulatory, hydroelectrolytic and pulmonary complications if used inappropriately. Another problem may result from the impaired positioning of the patients in those beds [39, 60].

Bleeding complications

Due to mucosal vulnerability, severe bleeding complications should be expected in any mucosal structure (Fig. 6). Generally, coagulation factors and blood counts should be held within the normal ranges, and the transfusion of red cells, platelets and plasma products should be considered when appropriate. Anticoagulation should be reversed in cases of persistent severe bleeding. Even minor manipulations, such as the placement of nasal tubes for enteral nutrition or laryngoscopy for endotracheal intubation, may result in life-threatening hemorrhaging and could compromise the ability to intubate or ventilate the patient. If airway pressure and oxygenation is increasingly affected, careful bronchoscopy may reveal, but may also provoke, tracheal hemorrhaging. Endoscopic adrenaline application, removal of debris and clipping of visible bleeding sources should be performed by those with expertise in this field. Pulmonary involvement in

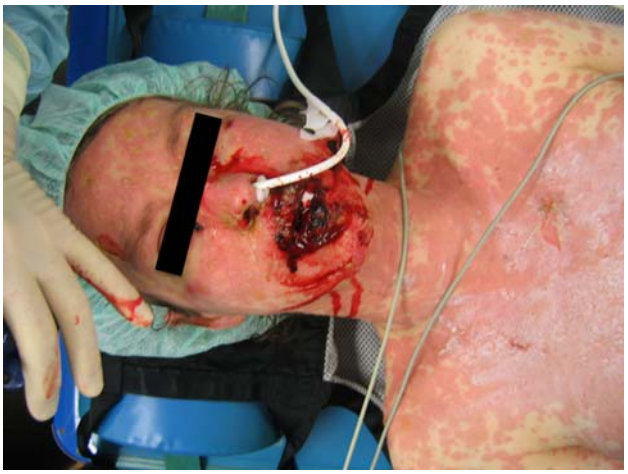

Fig. 6 Due to mucosal vulnerability, severe bleeding complications should be expected in any mucosal structure. Even minor manipulations could compromise the ability to intubate or ventilate the patient when oral mucosa, including the lips and the tongue, is affected by progressive mucosal sloughing

severe blistering diseases significantly influences their outcome [16, 61–64]. Oral or nasal bleeding should be treated with special mechanical tamponades, local application of adrenaline and clotting agents, and may require electrocoagulation. Consultation by an otolaryngologist should be requested [65, 66]. Bleeding from enteral mucosal erosions is reported to be hazardous, and timely endoscopic management should be initiated [39, 67, 68].

Healing process

The acute epidermolytic phase usually lasts no longer than 2 or 3 weeks. The beginning of re-epithelization is recognized after several days, often simultaneously with ongoing skin detachment and epidermolysis in other parts of the body. The progression of the wound healing process depends on the individual complication rate. Impaired metabolism, infections, hypothermia and the administration of high-dose catecholamines and analgosedation may have detrimental effects on cutaneous and splanchnic microcirculation [69, 70]. The necessity of these medications should be assessed continuously using a multidisciplinary approach. Supportive physical therapy should be focused on a stable progression of mobilization. Frequent mental evaluation and support by psychologists may be beneficial for the healing process and should not be underestimated.

Sequelae

The development of symblepharon, severe inflammatory ocular damage with entropium and trichiasis often leads to visual dysfunction and blindness. Frequent ophthalmologic examination is required in order to prevent this negative outcome [71, 72]. In addition to lid care and the removal of adhesions, ocular treatment includes topical steroids, topical antibiotics and lubricants. Medical treatments, however, do little to arrest these problems, and repairing the damage after the acute phase is very difficult. The application of cryopreserved amniotic membrane to the ocular surface during the acute phase of the disease has shown promise in limiting destructive inflammation and long-term sequelae [73].

Pulmonary lesions due to injured respiratory epithelia and especially tracheo-laryngeal strictures have a great impact on the quality of life, if the patient survives such complications. These strictures may require multiple operative interventions in order to achieve functional rehabilitation, such as the abilities to eat and swallow, even years after the acute skin detachment [63].

Further organ involvement in the intensive care of SCARs may be glomerulonephritis and renal tubulus necrosis, hepatitis and hepatocellular necrosis. Other frequent long-term complications are cutaneous dyspigmentation, complete loss of nails and esophageal, urethral and anogenital strictures [1, 9, 59, 63].

Withdrawal and further use of medications

Many patients with SJS or TEN are elderly men and women with underlying conditions that require medical treatment. Not all medications, therefore, can or should be stopped if an adverse reaction to drugs is suspected. On the other hand, early withdrawal of the culprit drug has been shown to improve the outcome of SCAR patients [74, 75]. In case the culprit drug or drugs have not yet been identified at the time of referral, it is important to obtain information on the patient's drug history. The risk estimation of epidemiologic studies can help to determine the associated drug(s) in the individual patient, since no reliable in vivo or in vitro tests exist to help identify the inducing agent [76]. Because SJS and TEN appear to be drug-specific, a patient usually develops the adverse reaction only after the use of one specific drug, which indicates that all other drugs needed for treatment of other problems can be continued.

Transport considerations

As described earlier, patients presenting with a SCAR are likely to be admitted first to regular medical, dermatological or emergency departments and are later transported to specialized intensive care units, which are most often burn centers. A successful transport phase is characterized by the thorough monitoring of all vital

functions, flexible and appropriate supportive treatment and the minimization of transport trauma [77, 78].

Respiratory competence should be assessed prior to transportation. Oxygen supplementation by mask is preferable to prophylactic endotracheal intubation if gas exchange is likely to be well maintained with spontaneous respiratory effort. If, however, there is altered consciousness, respiratory insufficiency or a likelihood of deterioration in the maintenance of respiratory sufficiency during transport, intubation should be performed in a controlled environment prior to transport. If the non-intubated patient requires sedation and analgesia for transport, medication should be used only with the highest caution and a continued clinical monitoring of respiratory function. Benzodiazepines, ketamine and opioids are not reported to exacerbate or trigger epidermolysis and may safely be used under these circumstances.

All non-vital medication (e.g., prophylactic antibiotics given by the referring hospital) should be avoided and discontinued until the diagnosis is confirmed and the inducing agent is identified.

Fluid therapy should be continued using crystalloids monitored via urinary output (0.5–1.0 ml/kg/h in adults, 1.0–2.0 ml/kg/h in infants). The infusion rate required depends on the patient's weight and the size of the TBSA affected by the skin detachment. We recommend 10–15 ml/kg/h as a basic fluid substitution rate during transport. Colloids should be avoided in the acute phase, although there is no evidence that they can induce SJS or TEN on their own. They may, however, cause pruritus and sometimes maculopapular skin eruptions [79]. Additionally, continuous catecholamine infusion may be necessary under transport conditions to maintain hemodynamic stability.

The patient should be moved deliberately with particular attention to the skin. As previously described, even a slight manipulation of the detached or denuded skin and mucosa may result in severe bleeding, which can be hazardous during transportation. If massive pharyngeal bleeding or epistaxis occurs during transport and no special nasal tamponades are available, gauze tamponades, soaked with vasoactive agents (e.g., adrenaline at a dilution from 1:10,000 to 1:1,000) or bladder catheters may be used for hemostatic compression [80]. Tachycardiac and hypertensive episodes caused by unintentional systemic adrenaline uptake and mucosal ulcerations by an aggressive and long duration of compression are potential side effects that have to be considered.

Transport-related hypothermia and shivering may result in decreased skin perfusion, the progression of cutaneous necrosis and coagulation disorders [39, 81]. Hypothermia, therefore, should be avoided. The patient should be covered with blankets, and direct wound dressings should be anti-adhesive and sterile. If possible, the air temperature of the ambulance or the helicopter cabin should be increased, and special rewarming devices should be employed during transport to prevent hypothermia.

Conclusion

We conclude that patients presenting with severe epidermolysis should be treated very carefully, in a manner similar to burn patients. Primary complications include respiratory and hemodynamic destabilization, mucosal bleeding and accidental hypothermia. The attending medical team should be aware of possible underlying diseases, instigating substances and altered immune defenses. Depending on the extent of epidermolysis and accompanying organ dysfunction, an emergency approach to these syndromes requires a thorough assessment of the medical history, appropriate hemodynamic support and oxygenation and analgesic therapy.

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