Introduction

Patients with severe burns (>20% total body surface area burn) are at risk for developing complications such as systemic infections and septic shock. The associated hemodynamic instability and perfusion failure might lead to the development of ischemic lesions that are unrelated to the burn injury. Ischemic necrosis of cutaneous and subcutaneous tissue is a serious complication in critically ill patients with a high mortality rate (up to 40%) and half of survivors require major reconstruction.1,2 We hereby present the case of a burn patient developing massive soft tissue necrosis after an episode of acute post-burn septic shock, with possible explanation of an overdosage of vasopressors due to significant body weight increase as an effect of the burn resuscitation. The utility of vasopressor agents in the management of septic shock depends on the balance between increased perfusion pressure and the direct effect on the microvasculature. The almost inevitable body weight increase in the acute post-burn phase as an effect of the resuscitation makes this balance more difficult to maintain.

Case description

A 42-year-old overweight (BMI 30.3) female sustained a fire injury from explosion of a grill and was admitted to our burn centre with a 50% total body surface area (TBSA) burn. Past medical history was significant for hepatitis C, alcohol, and drug abuse (oral). Deep partial-thickness and full-thickness burns were present on the face, neck, anterior thorax (partial sparing of breasts), whole abdominal area (deeper on epigastric, umbilical, right hypochondriac, and lumbar regions), bilateral upper arms (not including hands), bilateral anterior upper thighs, and gluteal regions (Fig. 1a,b). The patient was put under mechanical ventilation and was resuscitated accord-
ing to the Parkland Formula without any hypotensive episodes. Of note, an amount of 14.5 L resuscitation fluid was adminis-
tered within the first 7 hours only. Twenty-eight hours after the accident, the patient’s burns on the thorax and abdomen (16% TBSA) were enzymatically debrided (NexoBrid®). The treat-
ment with NexoBrid® proved to have good efficacy with the achievement of viable bleeding tissue covering the whole sur-
fase area (Fig. 2a,b). Wounds were subsequently covered with donor skin (allograft). She was taken to the operating room on days 3 and 6 for staged tangential excision and allograft appli-
cation to her neck, upper extremities, thighs and buttocks. The anterior neck was treated at the first session (day 3) to perform early tracheostomy. During this phase, the patient experienced an increase in body weight of +43% from admission (from 82 to 117 kg).

On day 4 she developed complications with a bloodstream infection and septic shock due to Streptococcus group C and Acinetobacter baumannii. Mean blood pressure was 50 mmHg and the patient was started on: high volume-fluid resuscitation (1000ml/h); antibiotic therapy (piperacillin-tazobactam, gen-
tamicin and clindamycin); and vasopressors (norepinephrine at 0.55 μg/kg/min and dobutamine at 6 μg/kg/min). After 13 hours of continuous infusion, the norepinephrine dose was lowered (0.35 μg/kg/min) and vasopressin (0.03 U/min) was added. Infusion of vasopressors continued for a total of 60 hours until she stabilized.

The patient returned to the operating room on day 8 for re-
vision of the thorax, abdomen and thighs. On removal of the allografts, the underlying tissue appeared diffusely necrotic on the right lateral thorax, right hemiabdomen and right inguinal region. Ischemic non-bleeding muscular tissue was exposed with evidence of thrombosed vessels. Necrosis also involved the external surface of the 7th-10th right rib (Fig. 3a,b). Speci-
mens of the tissue were sent both for culture and pathological examination; results from culture were negative; microscopic reports showed polymorphonuclear infiltration and edema of dermis, subcutaneous fat and superficial fascia, and angio-
thrombosis.

The debridement was semi-conservative with partial spar-
ing of the necrotic rectus abdominis to allow visceral coverage, and donor skin was applied on all wounds. Angio-computed tomography (angio-CT) scan of the torso on day 9 confirmed...
necrotic tissue to the right side of the abdomen and flank involving rectus abdominis, rectus transversus and obliquus externus abdominis muscles, with intact peritoneum, but no vascular thrombosis was detected.

Over the following two months, progressive demarcation and multiple debridements with resection of necrotic ribs left a defect of approximately 25 x 20 cm on the torso and 15 x 10 cm in the groin. The patient was reconstructed with pectoralis and latissimus dorsi pedicled fasciocutaneous flaps for the right thorax and abdomen, and a gracilis muscle pedicled flap for the inguinal region (Fig. 4a,b). After a few revisions, healing was completed and the patient was discharged on day 103 (Fig. 5).

Discussion

Subcutaneous tissue necrosis is an uncommon but severe complication of septic shock. Possible pathophysiologic mechanisms include: increased peripheral resistance; shunting of capillary exchange vessels; decreased delivery of O₂; impaired removal of CO₂; bacterial products activating the clotting mech-
Reduced skin necrosis typically occurs on fingers and toes, the relation to specific inotropic agents: while norepinephrine-in-platelets, spleen, testis and skin. The severity of lesions ranges from dry gangrene of vascular coagulopathy) and peripheral arterial occlusive dis-
vasopressors in critically ill patients, with only seven other re-
pressors as first-line therapy in septic shock. The most fre-
However, these agents also hold the potential to cause a num-
Ischemic skin necrosis is a rare complication of the use
vasopressors in critically ill patients, with only seven other re-
ports in the literature. Presumptive mechanisms include: extravasation, peripheral administration and high dose infu-
Complications have also been associated with infusion through a central venous catheter, the presence of risk factors (such as acute kidney failure, obesity, disseminated intravascular coagulopathy) and peripheral arterial occlusive dis-
The severity of lesions ranges from dry gangrene of the fingers and toes to extensive bruises and large exudative blisters on extremities. Cho et al. recently reviewed the ex-
isting reports of skin necrosis due to vasopressors in the liter-
ature, highlighting how lesions appear in different areas in relation to specific inotropic agents: while norepinephrine-induced skin necrosis typically occurs on fingers and toes, the wider areas of skin are more affected by vasopressin. This is related to the unique distribution of vasopressin receptor type 1 (V1 receptor), which is located in smooth muscles of the blood vessels, mainly in the territory of the splanchnic circulation, kidney, myometrium, bladder, adipocytes, hepatocytes, platelets, spleen, testis and skin. In our case, vasopressors were infused centrally through the subclavian vein and there was no extravasation. The patient was morbidly obese, but did not develop AKI/DIC. A combined therapy of inotropic agents was required to maintain adequate mean arterial pressure levels in the critical phase and vasopressors were administered in standard doses. However, the patient might have been exposed to an over-dosage of inotropic agents imputable to the significant weight gain (+43%) experienced in the resuscitative phase. On the other hand, the distributive and hypovolemic shock characterizing the acute post-burn phase might have contributed to the development of ischemic lesions through an additional decrease of blood flow to the tissues. Additionally, it must be noted that we extended the enzymatic debridement to 16% TBSA. While current posology and method of administration of NexoBrid now states that it should not be applied to more than 15%, developing a large raw area with considerable bleeding and fluid loss might have a side role in the development of hypotension. The pathophysiologic mechanisms involved the differential diagnosis of this complication included necrotizing soft tissue infection (NSTI), which was in accordance with significant positive fluid balance within the days before septic shock presentation and failure of all allografts. Diagnosing NSTI is very challenging in an acute burn patient and cannot be ruled out completely, as pathognomonic clinical findings (rubor, blistering, crepitations, pain out of proportion) are blurred in extensive burn injuries. Nonetheless, NSTI seems improbable in the present case, due to the following considerations:

- NSTI following burn injuries cannot be regarded as especially common in general, and it is even more scarce in Scandinavian countries (no reports of NSTI in burn patients in Scandinavia);
- at admission, the clinical picture could all be explained by the burn injury itself;
- LRINEC score on the day of development of septic shock = 7 (Intermediate Risk for Necrotizing Soft Tissue Infection); a biopsy from the pubic region was taken for culture of keratinocytes, and they grew adequately;
- there was no detection of foul smell, no dish-water fluid, no grey tissue but just dry, dead muscle and fat;
- necrosis of bones (ribs) is not a common feature in NSTI - more characteristic of coagulation/thrombi;
- history of drug abuse was not intravenous.

**Conclusion**

In the management of septic shock, special attention needs to be focused on the high treatment dose of vasopressors and the ability of these agents to reduce organ and tissue blood flow through their vasoconstrictive actions. The utility of these agents depends on the balance between increased specific perfusion pressure and the direct effect on the microvasculature. Body weight increase in the acute post burn phase as an effect of the resuscitation makes this balance more difficult to maintain. Guidelines for vasopressor dose calculation - adjustment in burn patients with septic shock are advocated.

**BIBLIOGRAPHY**


