Case Report

A case of toxic epidermal necrolysis comorbid with severe burns

Erina Miyano, Yuichi Horikoshi, Miyabi Nakayama, Tatsuki Kuroshima, Yuka Eto, Daisuke Kawata, Motoi Okada, Naohiro Kokita, and Satoshi Fujita

Department of Emergency Medicine, Asahikawa Medical University, Asahikawa, Japan

Background: Toxic epidermal necrolysis (TEN) and severe burns both have high mortality rates, but coexistence is extremely rare. The specificity of developing TEN in burn patients is not well understood and its treatment strategy is not established.

Case Presentation: A 68-year-old man was carried to our hospital with severe burns covering 35% of his body surface area. He developed bacteremia during treatment of burns and required antimicrobial therapy. However, erythema appeared on the trunk and upper limbs and rapidly spread to the extremities, leading to a diagnosis of TEN. The rash gradually improved after terminating antimicrobial therapy and administrating of 1,000 mg/day methylprednisolone for 3 days. The rash caused by TEN was confined to non-burned areas, suggesting that TEN may less likely occur at burn sites.

Conclusion: It is necessary to pay attention because burn patients can develop TEN concomitantly. Corticosteroids therapy may be effective for TEN even in severe burn patients.

Key words: Burn-site infection, mesh skin grafting, steroid-pulse therapy, suicide attempt, toxic epidermal necrolysis

BACKGROUND

TOXIC EPIDERMAL NECROLYSIS (TEN) causes necrosis of the epidermal layer of the body, resulting in widespread erythema and erosions, and is caused by antimicrobial agents, anti-epileptic drugs, anti-inflammatory, and analgesic drugs. Patients with TEN are at high risk of bacterial infection, sepsis, and multiple organ failure, leading to a poor prognosis with high a 1-year mortality rate of ~49%. The determination of a causative agent immediately is strongly recommended, and patients should be admitted without delay to a burn center or intensive care unit (ICU).

The coexistence of TEN and severe burns are extremely rare, and there is only one case reported previously regarding TEN during treatment of severe burns. Systemic corticosteroid administration has been often used in the management of TEN, but it should be considered more carefully during treatment of severe burns because of the disadvantages, such as increase exacerbation of burn-site infections or graft failure. Therefore, the specificity including mechanism of pathogenesis or treatment strategy of TEN in burn patients is not understood. Here, we report a successful case of TEN under the treatment of severe burns.

CASE PRESENTATION

A 68-year-old male presented with entire body burns. He tried to commit suicide by burning himself on the riv-erb, and covered his head with 10-liters of gasoline and set himself on fire. He had a history of insomnia and anxiety. He had no history of allergic responses and no smoking history. Vital signs on admission were as follows; Glasgow Coma Scale 15 points, body temperature 35.8°C, heart rate 98 bpm, blood pressure 170/85 mm Hg, respiratory rate 20 bpm, and oxygen saturation 100% with 10-liter mask. Erythema and bullae were observed on the auricular to mandible neck, thorax, abdomen, occiput, right upper arm, right dorsal hand, and left forearm. His anterior chest and posterior neck were covered with soot, and the skin in these areas had turned a grayish white (Fig. 1A). Soot was...
observed in the nasal and oral cavity, pharynx, and larynx, suggesting burn of the upper respiratory tract. Bronchoscopy showed soot adhesion, peripheral edema, and mucosal redness from the vocal cords to the period. Total burn surface area was 35%, which included 20% second-degree burns and 15% third-degree burns. The revised BAUX score was 120.

An overview of the hospital is shown in Figure 2. The burn-site was washed daily with warm water, treated with dimethyl isopropylazulene and gentamicin sulfate ointment and protected with moist wound care pads. At the time of admission, the guarantor’s approval was not obtained, which prevented aggressive initial burn treatment such as debridement and skin grafting.

On day 8, he had a high fever of 38°C–40°C with a markedly increased inflammatory response, and the blood culture revealed methicillin-resistant Staphylococcus aureus. Vancomycin and ampicillin/sulbactam were administered empirically against the burn-site infections. After the infections were under the control, the first split-thickness skin grafts (STSG) were performed on day 17 in the operating room. The skin grafts (0.01 inch graft) were harvested from the healthy skin on both thighs by using electric dermatome and meshed for expansion at the ratio of 1:3. After the first debridement and STSG on day 17, ampicillin/sulbactam was discontinued because of the appearance of erythema mainly on the lateral abdomen and suspected drug rash. Cefepime dihydrochloride hydrate was driven to start because acinetobacter baumannii was detected from a blood culture on day 20. Because the burn-site infections had been continuously manageable, the second STSG for the back area was performed on day 24. The skin was harvested from both lateral thighs and meshed at a ratio of 1:1.5.

From day 30, the redness on the trunk and extremities rapidly worsened, and some blistering was observed. We diagnosed as erythema multiforme because of drug eruption, then all antimicrobial agents were terminated. Because the erythema multiforme did not improve after the discontinuation of antimicrobial therapy, systemic administration of 40 mg/day prednisolone was initiated. However, on day 35, the erythema expanded and erosions and blisters formed on

Fig. 1. Skin images during intensive care unit (ICU) admission. Soot was observed mainly on his anterior chest and neck, and skin had turned grayish white, suggesting third-degree burns on the admission day (A). Erythema multiforme was seen in the anterior thorax. Erosion of the buttocks appeared and Nikolsky’s phenomenon was positive on day 30 (B,C). Improvement of erythema multiforme and erosion on trunk and buttocks were observed after steroid-pulse therapy on day 37 (D,E). Successful engraftment after five times skin grafting on day 120 (F).
more than 30% of the body surface area. Nikolsky phenomenon and oral mucosal lesions were observed, especially on the back and extremities (Fig. 1B,C). Because erythema, blisters, and erosions were widely distributed and exceeded 10% of the body surface area with a fever above 38°C, we diagnosed the case as TEN and initiated steroid-pulse therapy (methylprednisolone 1,000 mg/day) for 3 days. This treatment was successful and the erosions and blisters gradually improved without any exacerbation of infection. On day 37, the erythema began to fade (Fig. 1D, E). On day 38, we switched the steroids therapy to oral prednisolone 60 mg/day. Prednisolone was tapered by 10 mg every week. No signs of infection was observed after discontinuation of antimicrobial therapy and steroid pulse therapy, and he discharged from ICU on day 41.

Thereafter, an additional debridement for the anterior thoracic region on day 59, STSG for anterior neck, shoulder, and thoracic (from lower abdomen skin) on day 73, and STSG for lateral neck (from posterior aspect of both thighs) on day 87 were performed under general anesthesia (Fig. 1F). After debridement and skin grafting for a total of five times, he was transferred to a general hospital on day 140. Lymphocyte stimulation test of the antibiotics used was performed to search for the cause of TEN, but it could not be identified.

DISCUSSION

We experienced a rare case of TEN during the treatment of severe burns. The burn sites in the present case were neck, anterior thoracic, and posterior neck, but the site of TEN was confined to the non-burned site or the non-skin graft site. A previous report has also stated that the site of the onset of TEN is different from the burn site, and the burn site cannot be the subject of TEN.3 There are two possible reasons for this interesting phenomenon. First, TEN is caused by the release of granulysin from activated CD8-positive T lymphocytes and natural killer (NK) cells, activation of Fas by soluble Fas ligand (FasL) and total epidermal necrosis by tumor necrosis factor (TNF)-R1, DR4, DR5, and their ligands TNF-α and TRAIL.4 Therefore, TEN does not occur at the burn site beyond the epidermis, because there is no epidermis that is a likely target for TEN.
Second, it is known that T lymphocytes and NK cells are reduced at burn sites and the expression of CD8-positive T lymphocytes is said to be suppressed for more than 1 year in humans after burn injury, leading to reduced immunity and susceptibility to wound infection. Therefore, the skin immune response should be weak at the site of severe burns. In addition, even if they are targeted by TEN, TEN is less likely to be severe, especially in the acute phase, because T lymphocytes and NK cells are depleted. For the same reason, they may not be a target for TEN after skin grafts.

Severe burns and TEN require immediate therapeutic intervention because of the high mortality rate; treatment of TEN usually consists of early discontinuation of the causative agent and the systemic administration of corticosteroids. Moreover, corticosteroids prolong the healing period by exacerbating infection and severe gastrointestinal hemorrhage. Recent retrospective analysis revealed corticosteroids therapy following major burn injury was associated with higher in-hospital mortality, multi-organ failure, and sepsis. We closely observed the skin at the burn site for the presence of infection and consequently avoided complications from the use of corticosteroids. Physicians should pay meticulous attention to the steroid administration to TEN, especially with patients associated with severe burns. Further reports and studies are needed because of the lack of evidence.

CONCLUSION

Severe burns and TEN can coexist. It is necessary to keep in mind the onset of TEN even in burn patients. Corticosteroids therapy would be a potential treatment strategy for TEN in severe burn patients.

ACKNOWLEDGEMENTS

We thank Professor and Chair Akemi Yamamoto and her colleagues at Asahikawa Medical University for their cooperation.

REFERENCES

1. Anne M, Christopher G, David J et al. Bacterial infections after burn injuries: impact of multidrug resistance. Clin. Infect. Dis. 2017; 65: 2130–6.
2. Creamer D, Walsh SA, Dziewulski P et al. U.K. guidelines for the management of Stevens–Johnson syndrome/toxic epidermal necrolysis in adults 2016. Br. J. Dermatol. 2016; 174: 1194–227.
3. Conacannon E, Kennedy S, Shelley O. Toxic epidermal necrolysis after acute burn injury. Ann. Burns and Fire Disasters. 2018; 31: 266–70.
4. Elisabeth de A, Valerie D, Genevieve L et al. Death ligand TRAIL, secreted by CD1a+ and CD14+ cells in blister fluids, is involved in killing keratinocytes in toxic epidermal necrolysis. Exp. Dermatol. 2011; 20: 107–12.
5. Peng W, Zexin Z, Bin Y et al. Identifying changes in immune cells and constructing prognostic models using immune-related genes in post-burn immunosuppression. PeerJ 2022; 10: e12680.
6. Nadine B, Huber F, Marc H et al. Scald injury-induced T cell dysfunction can be mitigated by Gr1+ cell depletion and blockage of CD47/CD172a signaling. Front. Immunol. 2020; 11: 876.
7. Olivia C, Victoria H, Kevin P et al. Toxic epidermal necrolysis and Steven-Johnson Syndrome. A comprehensive review. Adv. Wound Care. 2020; 9: 426–39.
8. Khaled A, Poh T, Animesh A et al. Differential benefits of steroid therapies in adults following major burn injury. J. Plast. Reconstr. Aesthet. Surg. 2022; 75: 2616–24.

Animal Studies: N/A.
Conflict of Interest: None declared.

DISCLOSURE

APPROVAL OF THE Research Protocol: Not applicable
Informed Consent: Yes.
Registry and Registration No. of the Study/Trial: N/A.