

CASE REPORT

REGIONAL ANESTHESIA

Anesthetic management of toxic epidermal necrolysis: a report of two cases

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Abstract

Toxic epidermal necrolysis (TEN), is an acute, life-threatening emergent disease involving the skin and mucous membranes with serious systemic complications. It is characterized by widespread epidermal sloughing. Drugs are the most common triggers of TEN, but infection, vaccination, radiation therapy and malignant neoplasms can all induce it in susceptible patients. We report two cases in whom a hair dye and a COVID-19 vaccine (BioNTech®, Pfizer) were believed to be the causative agents. These patients have to undergo repeated debridements of the necrotic tissue. In this manuscript the anesthetic management of TEN patients is discussed. Detailed preoperative evaluation, aggressive fluid and electrolyte replacement, avoidance of hypothermia during debridement, minimizing anesthetic agents and limiting traumatic procedures are key points in the management.

Abbreviations: BUN: blood urea nitrogen; BSA: Body surface area; Cr: Creatinine; OR: Operating room; SJS: Stevens-Johnson Syndrome; TEN: Toxic epidermal necrolysis

Key words: Anesthesia; COVID-19; Toxic epidermal necrolysis; Vaccine

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1. Introduction

Toxic epidermal necrolysis (TEN), is an acute, life-threatening emergent disease involving the skin and mucous membranes with serious systemic complications. It is characterized by widespread epidermal necrolysis and sloughing.¹ Stevens-Johnson Syndrome (SJS) and TEN are considered to have the same pathophysiology and classified based on body surface area (BSA) involved. Patients are diagnosed with SJS, if less than 10% of their BSA is affected, while TEN needs 30% of the BSA or more to be affected. If the

range is between 10% and 30%, the patients are categorized as an overlap of SJS and TEN.¹ The cause of TEN in the majority of the patients is drug exposure and a resulting T-cell mediated type-IV hypersensitivity reaction. Drugs such as anti-epileptics, NSAIDs, allopurinol, antibiotics (e.g., trimethoprim-sulfamethoxazole, sulfonamides, cephalosporins), corticosteroids, infections, radiation therapy, malignant neoplasms and vaccination, can all induce TEN.^{1,2} It is a rare disease with an incidence of 1–2 cases per million persons per year with a mortality rate of 25–35%.² We discuss the anesthetic management of this rare entity in two cases.

2. Case Report 1

A 19-year-old female patient was transferred from another hospital to our Burn Unit because of peeling off the skin of her face, neck, thorax, back, upper and proximal lower extremities (Figure 1). She developed erythema and vesicles on her body followed by widespread sloughing off the skin, about 24 h after applying hair dye. She was hospitalized to our unit 24 h after the lesions had appeared. She had a history of arrhythmia and was on beta blockers. She was awake, agitated and alert. Her blood pressure (BP) was 115/74 mmHg, heart rate (HR) 125 beat per min (bpm) and temperature 37°C. She had a generalized, painful skin eruption with lesions of bullae to denuded skin areas. Her oral, nasal and pharyngeal mucosae were erythematous and edematous. The lesions involved 95% of the BSA. She had a Mallampati Class I airway. Serum level of sodium was 134 mEq/L, potassium 3.7 mEq/L, chloride 106 mEq/L and bicarbonate 19.2 mmol/L. The blood urea nitrogen (BUN) and creatinine (Cr) levels were 17 and 0.36 mg/dL respectively, glucose was 155 mg/dL, and hemoglobin (Hb) 13.2 g/dL. The electrocardiogram (ECG) showed sinus tachycardia. The patient was brought to the operating room (OR) for skin debridement. BP and oxygen saturation were recorded from lower extremities. Central venous catheter was inserted on right jugular vein since there was no intact skin area for venous access. Body temperature was measured through her ear every 5 min. We planned to apply deep sedo-analgesia, since her oral edema and facial lesions seemed to make it difficult to secure, insert and remove an endotracheal tube. Furthermore, we intended to avoid a burst of blebs, a damage on the larynx or bleeding inside the mouth. Anesthesia was conducted with midazolam, fentanyl, ketamine and propofol. Oxygen flow of 3L was applied nasally. The fluid replacement consisted of crystalloids at a rate to achieve a urine output of 0.5–1 ml/kg/h and a mean arterial blood pressure (MAP) of 60 mmHg. Room temperature was adjusted to 24°C, intravenous fluids were warmed and she was covered with warm sheets to prevent hypothermia. Her vital signs remained stable throughout the procedure. The desquamated skin was removed and BioBrane® synthetic skin dressing was applied over her back and Suprathel® temporary skin substitute over the remaining areas. The procedure lasted 90 min. Following an uneventful and short OR course, she was transferred to the Burn ICU. Intravenous morphine was used for postoperative pain. 10 days later she returned to the OR once more for debridement of 50% of the BSA and dressing changes. The patient consistently got better and was eventually transferred to dermatology clinic to get adjuvant therapy 17 days after

admission and discharged from hospital 20 days after transfer without any specific problem.



Figure 1: Skin sloughing on the back (Case 1)

3. Case Report 2

A 39-year-old woman was admitted to our Burn Unit, diagnosed with TEN after COVID-19 vaccination (BioNTech®, Pfizer). She had a widespread sloughing around 70% of BSA (Figure 2).

She had a history of atopic dermatitis and lactose allergy. She was awake, agitated and alert. Her BP was 151/77 mmHg, HR 68 bpm, and temperature 36.4°C. She had a generalized, painful eruption with lesions of bullae



Figure 2: Epidermal degloving of hands (Case 2)

to denuded areas. Her oral, nasal and pharyngeal mucosae were erythematous and edematous. She had a Mallampati Class I airway. Serum level of sodium was 133 mEq/L, potassium 4.3 mEq/L, chloride 103 mEq/L and bicarbonate 27.4 mEq/L. The BUN and Cr levels were 24 and 0.63 mg/dL, respectively. Blood glucose was 94 mg/dL, and Hb 12 g/dL. The ECG was normal. The patient came to the OR for skin debridement. BP and oxygen saturation were recorded from lower extremities. Central venous catheter was inserted on right jugular vein again in this case since there was no intact epidermal area for venous access. Body temperature was measured through her ear every 5 min. Oxygen flow of 3L was applied nasally. Under deep sedo-analgesia with midazolam, fentanyl, ketamine and propofol, the desquamated skin was removed and BioBrane®

synthetic skin dressing was applied over her back and gluteal areas. The remaining areas were covered with Suprathel® temporary skin substitute (Figure 3). Follow-up of the patient, fluid replacement, measures against hypothermia were the same as with case 1. There was no remarkable change in her vital signs. The procedure lasted for 60 min. Her disease progressed and she was taken to OR two more times for debridement and Suprathel® application to hands and lower extremities. She died on 10th day due to septic shock.



Figure 3: Face covered with Suprathel® (Case 2)

Both cases received methylprednisolone 1 mg/kg IV twice a day for 3 days on their admission and 3 g/kg Intravenous immune globulin for 3 days. They were both treated with cyclosporine 2.5–3 mg/kg/day. Case 2 also received plasmapheresis on the fifth day. Room temperature was maintained at 24°C and the patients covered with warm sheets to prevent the patients from hypothermia.

4. Discussion

The clinical features of TEN include a prodrome of fever and malaise for several days, followed by a rapidly progressing cutaneous lesions with mucosal involvement. Lesions are initially erythematous macules, or atypical target lesions on the trunk that progress to flaccid blisters with positive Nikolsky sign (detachment of the epidermis with light pressure) and sheets of denuded epidermis within days.^{1,3} Many of the patients have oral involvement with mucositis and ulceration. Ocular involvement occurs frequently with severe complications such as epithelial defects of the ocular surface or conjunctivitis with pseudomembrane.¹ Genitourinary involvement occurs in approximately one-third of TEN patients.³ Multisystem involvement necessitates early multidisciplinary involvement to help prevent sequelae of the disease.

Drugs, as mentioned before, are the most common triggers of TEN, but infection, vaccination, radiation therapy and malignant neoplasms can all induce TEN. In

our first case hair dye and in our second case COVID-19 vaccine (BioNTech®, Pfizer) were believed to be the cause of TEN.

Anesthetic management of TEN patients involves a detailed preoperative evaluation, aggressive fluid and electrolyte replacement, avoidance of hypothermia during debridement, effective postoperative pain control with opioids.

The skin lesions of the patients with TEN resemble those of patients with second-degree burns. On the other hand, the microvascular damage was reported to be less serious compared to burn patients requiring a less aggressive fluid replacement.⁴ The fluid requirements due to insensible losses through wounds were reported to be about 30% less in TEN patients than in burn patients with similar cutaneous involvement.^{1,5} Although there is an additional insensible loss through mucous membranes of various organs in TEN patients, the fluid replacement should be adjusted to aim a urine output of 0.5–1 ml/kg/h.^{1,5} Our fluid replacement in these cases consisted of crystalloids at a rate to achieve a urine output of 0.5–1 ml/kg/h and a mean arterial blood pressure of 60 mmHg. In case of hyponatremia, hypokalemia or hypophosphatemia, which frequently occur, replacement therapy is required.

The peripheral lines should be inserted over normal epidermis, if possible. Lines inserted through denuded dermis may play a role in bacterial entry.⁶ Unfortunately, there was no intact epidermis where we could insert a line, so we had to insert a central venous catheter on right jugular vein for fluid resuscitation and blood sampling in both of our cases. An arterial catheter is recommended for cases when it is impossible to use a blood pressure cuff or multiple blood samplings are foreseen. Since we were able to measure blood pressure from lower extremities, we did not consider an additional arterial access.

TEN not only invades the skin but also mucous membranes, so patient's oral cavity and airway should be examined for edema, erythema or ulcers. As both of our patients had face involvement, we planned not to apply face masks to prevent skin peeling. We also avoided intubation, not to cause a trauma like a bleeding inside the mouth, a burst of blebs or damage larynx. We decided to apply deep sedo-analgesia for the short procedures. Our main anesthetic choice was ketamine with minimal impact on cardiovascular and respiratory system, and strong analgesic effect. Anesthesia was conducted with midazolam, fentanyl, ketamine and propofol. Oxygen flow of 3L was applied nasally.

Dysphagia, excessive salivation, and painful oral ulcerations are encountered in early oral and upper airway involvement. The mucosal involvement can

extend down to the larynx, with inflammation and edema requiring endotracheal intubation. Bronchial epithelial detachment may result in lower respiratory tract obstruction, edema, infection, and atelectasis.³ Early pulmonary complications were found in 25% of cases. It was reported that respiratory symptoms related to bronchial epithelium detachment developed within 4 days after the onset of mucocutaneous symptoms. Bronchial involvement in TEN was not found to be correlated with the extent of epidermal detachment or with related drugs.⁷

TEN and SJS patients have been successfully taken to operations and debridement performed under general anesthesia with etomidate, ketamine, inhalation agents and total intravenous anesthesia.⁸⁻¹⁰ Endotracheal intubation and extubation should be performed cautiously to avoid any damage to the mucous membranes. Intraoral lesions and edema can be challenging. Smaller sized tubes and gentle suction before extubation may be helpful. Pleural blebs may rupture and lead to pneumothorax, for this reason airway pressures should be controlled, and high pressure and volume ventilation be avoided. Drugs like NSAID, antibiotics, anticonvulsants, barbiturates and sedatives which may precipitate TEN should be used cautiously. Postoperative pain can be managed with paracetamol, tramadol and opioids, avoiding NSAIDs.

TEN patients are prone to hypothermia. Measuring body temperature is necessary in TEN patients. It has been suggested that the OR temperature should reach 28°C.⁹ In our cases we were unable to control the temperature of our operating room because our hospital building has a central heating system. We could adjust the room temperature to 24°C. We used warmed intravenous fluids and covered our patients with warm sheets to prevent hypothermia. The durations of the surgeries were reasonable.

5. Conclusion

Since drugs play an important role in toxic epidermal necrolysis, it is important to minimize anesthetic agents and limit traumatic procedures. Anesthetists should keep in mind and be ready for the pulmonary complications such as pulmonary edema due to fluid overload, bacterial pneumonia, atelectasis, bronchial obstruction, bronchospasm and laryngospasm. Since these patients are prone to infections, special care should be given to prevent septicemia. Fluid replacement and precautions for hypothermia are important issues in anesthetic management.

6. Conflict of interest

The authors declare no conflicts of interest.

7. Authors' contribution

BT: Conduct of the cases, main writer, literature review

EE: Manuscript editing, corrections

GI: Literature review

MA: Conduct of the cases, manuscript editing

OK: Manuscript editing

8. References

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