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#### **ABOUT COVER**

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CASE REPORT

# Efficacy of borneol-gypsum in skin regeneration and pain control in toxic epidermal necrolysis: A case report

Lu-Wei Yang, Li-Juan Zhang, Bin-Bin Zhou, Xin-Yu Lin, Yu-Ting Chen, Xiao-Yu Qin, Hui-Ying Tian, Li-Li Ma, Ying Sun, Lin-Di Jiang

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### Abstract

#### BACKGROUND

Toxic epidermal necrolysis (TEN) is a life-threatening dermatological emergency mainly induced by drug hypersensitivity reactions. Standard management includes discontinuation of culprit drug and application of immunomodulatory therapy. However, mortality remains high due to complications like septic shock and multiorgan failures. Innovative approaches for skin care are crucial. This report introduces borneol-gypsum, a traditional Chinese drug but a novel dressing serving as an adjuvant of TEN therapy, might significantly improve skin conditions and patient outcomes in TEN.

#### CASE SUMMARY

A 38-year-old woman diagnosed with eosinophilic granulomatosis with polyangiitis experienced gangrenous complications and motor nerve involvement. After initial treatment of high-dose corticosteroids and cyclophosphamide, symptom of foot drop improved, absolute eosinophil counts decreased, while limb pain sustained. Duloxetine was added to alleviate her symptom. Subsequently, TEN developed. Additional topical application of borneol-gypsum dressing not only protected the skin lesions from infection but also significantly



eased localized pain. This approach demonstrated its merit in TEN management by promoting skin healing and potentially reducing infection risks.

#### **CONCLUSION**

Borneol-gypsum dressing is a promising adjuvant that could significantly improve TEN management, skin regeneration, and patient comfort.

Key Words: Toxic epidermal necrolysis; Eosinophilic granulomatosis with polyangiitis; Duloxetine; Borneol; Gypsum; Case report

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**Core Tip:** This case report highlights the innovative use of Borneol-Gypsum dressing in the skin management of toxic epidermal necrolysis (TEN). Despite the standard treatments, the patient's condition improved remarkably after supplementary application of this dressing, showcasing its potential in halting disease progression and fostering skin regeneration. The borneol-gypsum dressing not only relieved pain of exfoliated skin but enhanced patient cooperation during dress changing, suggesting it could be a promising dermatological supplement for further care in TEN.

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#### INTRODUCTION

Toxic epidermal necrolysis (TEN) is a severe skin injury most frequently caused by drugs and characterized by widespread necrosis and shedding of the skin. Secondary infections are a leading cause of TEN's high mortality rate of up to 30%[1]. Traditional treatment for TEN involves discontinuing all suspected drugs and administering high doses of glucocorticoids and human immunoglobulin. Recent studies have demonstrated that the use of tumour necrosis factor (TNF) antagonists can improve the prognosis of TEN patients. Proper skin care and skin barrier reconstruction also play crucial roles in reducing the risk of infections and further lowering the mortality rate[2-4]. Borneol, a component of traditional Chinese medicine, has been shown to have protective effects on the skin and to facilitate wound healing. Borneol targets the TRPM8 pathway to provide pain relief and promotes skin healing by reducing inflammation and activating the p38-COX-2-PGE2 signalling pathway [5,6]. A recent case study reported successful treatment of druginduced TEN through the use of traditional treatments, casting, and borneol application, resulting in improved survival rates and reduced infection risk.

#### CASE PRESENTATION

#### Chief complaints

Rash for one year, one-month foot drop, erythema and blisters for one week.

#### History of present illness

A 38-year-old female patient visited our Rheumatology Clinic complaining of recurrent itchy erythema on her lower limbs that had persisted for a year. A month before her admission, she experienced discolouration and severe pain in her right ring and little fingers, scoring 9 on the visual analogue scale, accompanied by limping and right foot drop. The patient's complete blood count indicated a significant increase in eosinophils, and ultrasonography of her limbs revealed multiple embolisms in both radial arteries, anterior tibial arteries, and dorsal foot arteries. Electromyography indicated peripheral nerve damage in multiple areas of both lower limbs, suggesting axonal degeneration. After excluding clonal haematological malignancies through bone marrow aspiration and biopsy, she was diagnosed with eosinophilic granulomatosis with polyangiitis (EGPA) based on the American College of Rheumatology/European League Against Rheumatism 2021 criteria. The patient began a comprehensive treatment regimen, which included intravenous methylprednisolone (1 g/d for 3 d, followed by 80 mg/d for another 3 d, which was subsequently orally tapered starting from 1 mg/kg/d), intravenous cyclophosphamide (0.8 g/month), oral warfarin, beraprost sodium, and vitamin  $B_{12}$ . Two weeks later, her foot drop improved, and there was no further progression of necrosis in her fingers, although her pain persisted. The patient was then discharged with a prescription of duloxetine for pain management. Three days postdischarge, she developed progressive red rashes on her limbs, chest, and abdomen, which evolved into large, ruptured, exudative blisters. Additionally, she experienced erosion and congestion in the mucous membranes of her lips and eyes,



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along with intensified pain, necessitating a return visit to the clinic.

#### History of past illness

The patient's medical history included bronchial asthma and allergic rhinitis.

#### Personal and family history

The patient had no significant personal or family history.

#### **Physical examination**

Upon admission, the patient had a temperature of 37.8 °C, a blood pressure of 99/53 mmHg, and a heart rate of 129 beats per minute. Oral examination revealed mucosal erosion and crusting with darkening of the lips. She exhibited diffuse, dark erythema on her face, along with ulcerative lesions on her eyelids. The conjunctiva was congested and exudative, while the cornea was still clear. Her trunk showed widespread erythema with lax blisters and bullae, some of which were ulcerated and eroded, and a positive Nikolsky sign was observed. The upper limbs were marked with multiple dark erythematous patches and blisters. On the patient's lower limbs, there were widespread erythematous patches and blisters and blisters were present on the soles of her feet. Notably, there was evident necrosis on her right ring and little fingers.

#### Laboratory examinations

Routine blood tests revealed a white blood cell count of  $13.81 \times 10^{\circ}/L$  (90.0% neutrophils,  $0.04 \times 10^{\circ}/L$  eosinophils), a haemoglobin level of 110 g/L, and a platelet count of  $451 \times 10^{\circ}/L$ . The faecal occult blood test was positive/negative. Liver function tests revealed alanine aminotransferase levels of 25 U/L, aspartate aminotransferase levels of 31 U/L, total bilirubin of 4.0 µmol/L, albumin of 29 g/L, and a blood glucose level of 11.2 mmol/L. The renal function parameters included a serum urea nitrogen concentration of 12.6 mmol/L and a creatinine concentration of 82 µmol/L. Her electrolyte levels were potassium 3.1 mmol/L, sodium 135 mmol/L, chloride 100 mmol/L, and serum bicarbonate 19 mmol/L. The erythrocyte sedimentation rate was 88 mm/h, and the hypersensitive C-reactive protein concentration was 30.6 mg/L. The serum amyloid A concentration was 525.0 mg/L. The cytokine levels were as follows: TNF, 55.80 pg/mL; interleukin (IL)-1 $\beta$ , 14.0 pg/mL; IL-2 receptor, 664.0 U/mL; and IL-6, 28.40 pg/mL. The procalcitonin concentration was 0.05 ng/mL. Blood cultures for aerobic and anaerobic bacteria were negative. The Score of TEN was calculated as 4.

#### Imaging examinations

The patient did not undergo any imaging studies as part of the diagnostic evaluation.

### FINAL DIAGNOSIS

TEN and EGPA.

#### TREATMENT

The suspected allergenic drug duloxetine was discontinued, and the room temperature was maintained between 28 and 30 °C. Following dermatological and ophthalmological consultations, the patient received a single dose of 500 mg methylprednisolone, which was tapered to 80 mg/d and adjusted to 40 mg/d after 6 d. This treatment was accompanied by 20 g/d of intravenous immunoglobulin for 5 d and an initial dose of 50 mg of recombinant human type II TNF receptor antibody fusion protein, followed by 25 mg every 3 d. Meropenem (1.5 g daily) was used for anti-infective therapy, and omeprazole (80 mg/d) was prescribed for stress ulcer prevention. The patient's hydration and nutritional needs were addressed with 3500-4000 mL of 0.9% saline solution daily, along with a high-calorie, protein-rich liquid diet. Rigorous monitoring of blood glucose levels ensured that the levels remained within acceptable ranges. Ophthalmological care included bidaily administration of tobramycin and dexamethasone eye drops supplemented with twice-daily carbomer eye gel and four daily polyvinyl alcohol applications to both eyes. Daily saline washes were conducted for eye hygiene, and mupirocin ointment was applied to the lips thrice daily. Extensive blisters on the limbs and trunk were managed with fluid drainage, and regular saline washes were used for cleansing the skin lesions. The affected regions were treated with a combination of mupirocin, petrolatum gauze, and povidone iodine gauze. Additionally, diluted potassium permanganate (1 g/8000 mL) was used for sitz baths. On days two and three, the patient experienced persistent serous discharge from the skin on the back, accompanied by considerable pain. The skin care regimen was adjusted to include mupirocin, petrolatum gauze, povidone iodine gauze, gypsum, and borneol on the ruptured areas. This adjustment led to a marked decrease in discharge and alleviation of pain. The treatment approach consisted of gypsum, borneol, mupirocin, petrolatum gauze, and povidone iodine gauze (Figure 1).

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Figure 1 Timeline of drug adjustment and skin lesion changes during the treatment process.

## **OUTCOME AND FOLLOW-UP**

By the fifth day, new skin had formed in the affected areas, prompting continued treatment with regular changes in the wound dressings. Significant improvement in the skin lesions was evident by the eighth day, at which point new skin growth occurred. By Days 12 to 14, the skin lesions had completely resolved. The patient has been under regular followup for a year, with no recurrence of skin lesions.

### DISCUSSION

TEN is a severe and potentially fatal disease caused by widespread shedding of the skin, severe systemic infection, toxic symptoms, and multiple-organ failure, leading to a high mortality rate[7]. Despite a lack of standard treatment, strong evidence supporting the use of glucocorticoid and human gamma globulin approaches is lacking. In recent years, TNF inhibitors (TNFis) have been tested for use in treating TEN, but large-scale data are still lacking[8]. Hence, proper supportive care and attentive nursing are crucial in treating TEN with the aim of reducing its mortality.

In this case, we treated the patient with TEN by an intensive immunosuppression regimen that included high-dose glucocorticoids and standard-dose TNFis. To improve the effectiveness of skincare, a combination of gypsum and borneol was used in combination for basic management. Borneol, a natural substance commonly used in food and traditional Chinese medicine for pain management and anaesthesia, has been shown to have anti-inflammatory effects, as well as the



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ability to reduce monocyte infiltration and the number of Th1 and Th17 cells[5,9,10]. Borneol also has antiadhesive properties, reducing bacterial attachment and biofilm formation, and can enhance the efficacy of antibiotics[11,12]. Moreover, borneol has been reported to inhibit oedema and severe skin erythema[6,13,14]. The use of gypsum, commonly used to treat scalds, has been shown to improve exudate absorption, wound healing, and muscle regeneration, and calcium ions play crucial roles in burn healing and anti-inflammatory effects [15-17]. The combination of gypsum and borneol effectively reduced local pain, facilitated skin lesion repair, reduced patient discomfort, improved patient compliance with dressing changes, and reduced the risk of infection. This approach may be an important treatment strategy for patients with TENs.

Overall, more attention should be given to the prevention of TENs in the management of patients with EGPA. A history of allergy and high levels of eosinophilic granulocytes are the prominent features of EGPA, leading to high frequencies of allergic reactions in patients with EGPA. Regular visits, health education, careful physical examination and drug monitoring may help to reduce the incidence of TEN.

#### CONCLUSION

TEN, a serious skin injury, can be managed more effectively by adding recombinant human TNF receptor II antibody fusion protein and borneol-gypsum dressings to conventional therapy. This approach not only controls disease progression and fosters skin regeneration, but it also minimizes local pain and enhances patient compliance, which potentially reduces infection risks.

#### FOOTNOTES

Author contributions: Yang LW participated in the clinical treatment of patients, performed the analysis, and wrote the manuscript, leading the main contributions to this work; Zhang LJ, Zhou BB, Lin XY, Chen YT, Qin XY, and Tian HY contributed equally to this work; Ma LL, Sun Y, and Jiang LD provided guidance for the work and analytical direction; All authors have read and approved the final manuscript.

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