Toxic epidermal necrolysis (TEN) after sclerosing tissue glue injection in oesophageal variceal ligation in patients with liver malignant tumors: A case report

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Case Report

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Abstract

Background

Toxic epidermal necrolysis (TEN) is one of the few allergic diseases with an acute onset and severe symptoms in dermatology. Drugs are the most important pathogenic factors for this condition. Referring to the relevant literature, TEN after endoscopic surgery has been rarely reported.

Case presentation:

A 58-year-old male patient with chronic liver disease was treated with oesophageal variceal ligation, sclerosing agent and tissue glue injection due to oesophageal and gastric variceal bleeding. After 2 days, the patient's skin exhibited erythema to different degrees. After 10 days of dexamethasone treatment, the whole-body rash worsened, and a severe skin reaction appeared, which was suggestive of toxic epidermal necrolysis (TEN). Strict mucosal care was provided, and corticosteroids, gamma globulin and adalimumab were concurrently used for treatment. After 20 days, the patient recovered from the skin problems.

Conclusion

Combined with domestic and international case reports, this may be the first case report of toxic epidermal necrolysis after sclerosing tissue glue injection in oesophageal variceal ligation. When patients with multiple drugs have multiline erythema, physicians should be alert to the possibility of its development into TEN. This article summarizes the experiences of this patient and related diagnoses and treatments at home and abroad, which provides a practical clinical basis and experience for the diagnosis and treatment of TEN in the future.

1. Introduction

Toxic epidermal necrolysis (TEN) is one of the few allergic diseases with an acute onset and severe symptoms in dermatology. The incidence rate is low, but the mortality rate can reach approximately 61% [1]. Drugs are the most important pathogenic factors for this condition. Some antibiotics, such as sulfonamide and penicillin, as well as some psychotropic drugs, such as barbiturates and phenytoin, have been occasionally reported to cause TEN. However, the pathogenic factors of TEN not only include drugs but also include other special factors. The onset of TEN is typical, with local erythema of the body at the initial stage, accompanied by pain. In a short period of time, the disease can rapidly develop from erythema to bullous skin lesions, after which peeled skin tissues can appear. During patient care, external forces (rubbing or squeezing) can cause patches of bullous skin to peel off (which is known as the Nikolsky sign), and the peeled wound is similar to a 2nd degree scald. The skin stripping area is an important index to evaluate TEN. According to the percentage of skin stripping area compared to the...
whole body surface area, the disease is referred to by different names. A ratio below 10% refers to Stevens-Johnson syndrome (SJS), a ratio above 30% refers to TEN and a ratio higher than 10% but lower than 30% refers to overlapping SJS to TEN. In addition to skin symptoms, there can also be systemic symptoms, such as fever, fatigue, chills and muscle soreness. Exfoliation can also occur in other parts of the mucosa, such as in the eyes, lips and external genitalia. If the disorder is combined with the exfoliation of other parts of the mucosa, it indicates that the condition has become extremely serious. If the disorder is not properly treated, patients are prone to electrolyte disturbances and can even die due to the dysfunction of multiple organs.

2. Case Report

A 58-year-old male patient was hospitalized on April 23rd because of haematemesis and black stool being experienced for one day. Preliminary diagnoses included oesophageal and gastric variceal bleeding, decompensation of posthepatitic cirrhosis, chronic hepatitis B, anaemia, ascites, spleen enlargement, liver malignant tumour, portal vein embolism and portal hypertension. After admission, the patient was treated with Losec for acid inhibition, stanine and terlivasopressin for increased pressure, furosemide for diuresis, polyene phosphatidylcholine for liver protection and rehydration.

Diagnosis and treatment. On April 29th, the patient underwent endoscopic surgery with the use of a venous ligation ring, sclerosing agent (10 mL polycinnamon) and tissue glue (2 mL Compait). On May 1st, the patient developed a scattered rash with itching; therefore, he stopped using stanine for injections and instead used an octreotide needle. Dexamethasone (5–10 mg/day) was used for symptomatic treatment via an intravenous drip to relieve the allergies. On May 3rd, the number of rashes increased, and mild erosion of the lips appeared. Dermatologists diagnosed erythema multiforme according to the current situation. When considering drug allergies, the patient denied a history of antipyretic and analgesic drugs, anti-inflammatory drugs, new drugs or sensitizing drugs within one month before admission. Dexamethasone was stopped, and a methylprednisolone needle (60–80 mg/day) was used. On May 12th, the blisters on the back of the patient increased in number, and the flaky range also increased. Furthermore, part of the skin became exfoliated, the wound was eroded and the Nissl's sign was positive (Fig. 1A-C). The laboratory examination results showed that IgG levels were 24.85 g/L, IgA levels were 0.3 g/L and other immunoglobulin levels were generally normal. In addition, the patient's lip mucosa was damaged, the oral mucosa was eroded to varying degrees, the conjunctiva was congested and a small amount of secretion appeared. Combined with the abovementioned symptoms, the revised diagnosis was toxic epidermal necrolysis. When considering that patients with upper gastrointestinal bleeding should not use an excessive dose of corticosteroids, gamma globulin (20 g/day) and methylprednisolone (100 mg/day) were administered, omeprazole sodium and octreotide injection were stopped and oral rabeprazole sodium enteric-coated tablets (20 mg/day) were used for symptomatic treatment. After 4 days, the rash still had not obviously improved, and the erosion and exfoliation of the trunk skin were worse than before (with obvious pain). Adalimumab (40 mg/day) was subcutaneously injected on May 16th, and the wound was wet applied with Kangfu New Liquid gauze (Fig. 2). After 2
days, the rash had obviously improved. On May 20th, the wound was dry, and some of the scab skin fell off (Fig. 3). After 10 days (May 30th), the rash had generally recovered (Fig. 4). Other diseases continued to be treated via specialist symptomatic treatments.

3. Treatment Experience

3.1 The treatment of TEN should be considered from many aspects, and the combination treatment of various methods should be initiated as soon as possible \[4\], which should not only avoid the existence of pathogenic factors but should also alleviate the clinical symptoms of patients and strengthen the life support of patients \[5\]. Care for skin lesions should be provided with more attention on avoiding iatrogenic secondary injuries.

3.2 Stopping the pathogenic factors. Hypersensitivity is an important pathogenesis of TEN, and it is very important to stop the factors inducing TEN. When our patient was diagnosed with TEN, he stopped using many suspicious drugs, but the sclerosing agent and tissue glue that were used in this operation could not be removed. Garcia-Doval et al. retrospectively studied the clinical data of 113 patients with SJS or TEN and theorized that the immediate cessation of sensitizing factors (drugs) could significantly reduce the mortality of patients \[6\].

3.3 Life support. TEN progresses rapidly; additionally, with the aggravation of patients’ conditions, skin damage will be further aggravated (progressing from SJS to TEN). Bullous skin lesions and large areas of epidermis peeling, as well as exudate on the skin surface, may increase; additionally, the condition can also lead to the loss of body fluids in patients. At this point in time, special attention should be given to the patient's bodily fluids and electrolytes, timely symptomatic treatments and the maintenance of stability \[7\]. This patient not only suffered from a bloody emergency of the digestive tract but was also in the end stage of chronic liver disease; therefore, the stability of bodily fluids and electrolyte balance was more important. In this scenario, physicians should improve the immune function of patients and avoid aggravating the disease due to complications. In addition, the relief of patients’ pain is also an important treatment link, and proper use of analgesic drugs can improve their quality of life \[8\].

3.4 Symptomatic treatment of skin lesions and mucous membranes. The exudate from the patient's skin surface can coagulate and cover the skin, which can then easily cause skin infections. Therefore, these exudates should be carefully removed during nursing, and the healing skin lesions that affect erosion should be treated in a timely manner to minimize the possibility of skin infections. In this case, the patient is covered with Vaseline gauze after the external application of antibiotic ointment, which can not only resist bacteria but can also prevent adhesion, as well as better protecting the wound surface. Wet compresses with gauze of Kangfu New Liquid of Traditional Chinese Medicine can be used to promote skin healing. If there are eye secretions, antibiotics and glucocorticoid eye drops that do not easily cause allergies can be properly used. Moreover, mucous membrane damage in the oral cavity can be gargled with the traditional Chinese medicine Kangfu New Liquid, and antibiotic ointment can be applied to the lips to protect the wound surface and to resist skin infections.
3.5 Prevention and control of infection. The skin is a protective barrier of the human body. TEN patients lack this important defensive barrier, which is easily invaded by bacteria and causes nosocomial infections, as well as possible septicemia (one of the most common and serious complications of TEN patients) [9]. If TEN patients are complicated with septicaemia, it is a very difficult problem to manage. Therefore, attention should be given to the identification of potential infection factors during patient care. In addition to regular disinfection and dressing changes in wounds, various pipelines (nasal feeding tubes, urinary catheters and other indwelling arterial and venous catheters, among other factors) also need to be disinfected in a timely manner. Although it is necessary to prevent patients from becoming infected, preventive use of antibiotics is not advocated. Therefore, in the examination of patients, the indicators of early infection should be found in a timely manner, after which antibiotics that are not allergic in nature should be selected (according to drug sensitivity cultures).

3.6 Glucocorticoid therapy. In this case, dexamethasone was used for the antiallergic treatment when the rash appeared on May 1st. Glucocorticoids have been used to treat allergic diseases for decades. A case study of 281 cases of SJS or TEN in France and Germany showed that if glucocorticoid pulse therapy was used, the mortality of SJS or TEN patients could be greatly reduced. In addition, Stefanie Zimmermann et al. [10] considered glucocorticoids to be the most promising systemic immunomodulatory therapy for SJS/TEN in 96 studies (3,248 patients).

3.7 Immunosuppressive therapy. Immunosuppressants are used in many disciplines and diseases, and their medication range is wide. The drugs that are commonly used to treat SJS/TEN are infliximab and adalimumab. Researchers have found that infliximab can quickly control the disease when treating TEN [11]; in addition, skin lesions and systemic symptoms are rapidly relieved, recovery is better, the mortality rate is low and adverse reactions are rare. However, infliximab is still a heterogeneous antigen for the human body and is a chimeric IgG1 antibody against TNF-α. Wan Hongcheng and other scholars believe that it is better to use adalimumab to treat SJS or TEN. In other fields, Wei Da has reported cases of switching to adalimumab after failure to treat Crohn's disease with infliximab [12].

3.8 Chinese medicine treatment. In this case, when treating the erosive skin lesions, the traditional Chinese medicine Kangfuxin Liquid was applied, which belongs to the class of traditional Chinese medicine. After drying the worms of *P. americana*, the effective medicinal components were extracted [13]. Clinical studies by Wu Mingming et al. found that kangfuxin liquid can effectively inhibit bacterial reproduction, relieve inflammatory reactions, relieve swelling and pain, effectively control exudation, promote healing and shorten the course of the disease [14]. Kangfuxin liquid can also promote mucosal repair and has a good repair effect on TEN complicated with oral mucosal damage.

3.9 Human immunoglobulin. The efficacy of intravenous human immunoglobulin on SJS/TEN is controversial. Stacy J Barron et al. found that the intravenous injection of human immunoglobulin (≥ 2 g/kg) may improve the treatment of SJS/TEN, but further scientific research is needed to confirm this hypothesis [15]. Huang Yucheng et al. believed that this therapy has little effect on TEN (even if high doses are used) [16]. Moreover, Yang Yongsheng et al. believed that the combination treatment of glucocorticoids and intravenous human immunoglobulin has a tendency to reduce the mortality of SJS/TEN patients, but the decrease in mortality was statistically non-significant. The combined use of
glucocorticoids and intravenous human immunoglobulin to treat SJS/TEN can control the progression of skin lesions at an early stage and shorten the hospitalization time of patients, thus indicating that the total dose of glucocorticoids will be reduced; however, the early dosage of glucocorticoids has no effect [17].

3.10 Cyclosporine. Cyclosporine is mainly used in the clinic to inhibit the activation of T cells and macrophages via its immunosuppressive effects. In dermatology, cyclosporine is mainly used to treat psoriasis, atopic dermatitis, chronic idiopathic urticaria, pyoderma gangrenosum, bullous dermatitis, systemic lupus erythematosus, drug eruption and other conditions. Raqiya Al Rajaibi has reported of the treatment of TEN with oral cyclosporine [18]. At present, cyclosporine is rarely used as the first-line drug for TEN.

3.11 Other drugs. Cyclophosphamide and thalidomide have been used to treat SJS/TEN, but there have been few recent reports, which may be related to its slow onset time and considerable side effects. However, it still exerts its curative effect in the treatment of other diseases, such as multiple myeloma and Crohn's disease.

3.12 Plasma exchange technology. Plasma exchange is a blood purification method in which the blood in the body is isolated, the plasma or harmful substances in the plasma are separated by using various instruments and the same amount of replacement solution is returned to the body [19]. This procedure plays an important role in many disciplines. For example, plasma exchange therapy is often used as the last treatment after other methods of treatment of SJS/TEN are ineffective. Han F et al. reported of 17 TEN patients being cured via plasma exchange and provided a positive recommendation for plasma exchange. However, some scholars believe that there are still some problems in the treatment of TEN by the sole use of plasma exchange [20].

4. Discussion And Summary
This patient not only suffered from a blood emergency of the digestive tract but was also in the end stage of chronic liver disease. There are many types of drugs that are used after hospitalization; therefore, it is difficult to determine the uniqueness of the root cause of TEN. The date of the rash was on the second day after the operation, and the time point was the more important factor. However, the use time and rash time of omeprazole sodium for injection (Losec), somatostatin for injection (Sitanin) and terlipressin cannot be ignored.

On the 4th day after the occurrence of the rash, the patient was considered to have erythema multiforme, which is usually related to an infection. The typical skin lesions in the initial stage mainly involve erythema with different degrees of shooting target shapes (or iris shapes), which is a skin disease related to acute onset and inflammation that is usually accompanied by mucosal damage and which can heal itself; however, it can easily recur [4], and its mortality rate is obviously low. Inspired by the experiences of diagnosis and treatment of this case, if multiline erythema appears in patients with complicated medication usage, it is also necessary to be alert as to whether it is an important precursor of Stevens-Johnson syndrome or TEN.
TEN is a type of acute and severe allergic autoimmune skin reaction caused by infectious factors; it can also be caused by many other factors, but most of them involve drug factors. There are many studies on its pathogenesis at home and abroad, but there is no unified consensus on this pathogenesis. This patient developed a rash after 2 days of digestive endoscopy and rapidly developed TEN, which is rarely reported at home and abroad. In addition, life support treatments (such as rehydration, desensitization with glucocorticoids, wet compresses with gauze of kangfuxin liquid, erythromycin ointment to resist mucosal infections, intravenous injections of human gamma globulin to enhance the body's disease resistance and adalimumab, which is a TNF antagonist) can have obvious effects. On the basis of comprehensive treatment, adalimumab exerts its specific advantages, which results in the skin symptoms of patients becoming benign. In addition, if patients are initially treated with adalimumab when their skin exhibits multiline erythema, there is a question as to if the development of TEN can be controlled. In future clinical practice, we will continue to identify valuable cases for in-depth study, with the hope of obtaining new answers to this question.

**Declarations**

**Ethics approval and consent to participate**

As per the Academic Ethics Committee of Shaoxing People's Hospital, the case report does not require ethical approval or patient consent, as long as there are no interventions and patient identification in the report. Therefore, this case report does not require ethical approval or patient consent.

**Consent for publication**

Written informed consent was obtained from the relevant personal involved in this study for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

**Availability of data and materials**

Not applicable.

**Competing interests**

The authors declare that they have no competing interests.

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**Authors’ contributions**
LCH and WC: Collect the clinical case data, major contributor to the manuscript. XCG, QL and ZMZ: Provide guidance and check on the professional issues involved in the manuscript. HC, YHZ and JD: Check the professionalism of the manuscript and control the overall quality.

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Not applicable.

References


Figures
Figure 1

A Rash on the back shoulder and neck. B Exfoliation of skin on the back. C Exfoliation of surface layer of back skin
Figure 2

Kangfuxin Liquid gauze wet compress

Figure 3

Wound convergence and partial scab peeling.
Figure 4

The rash was basically cured