Hyperbaric oxygen treatment for toxic epidermal necrolysis: A case report

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Key words
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Abstract

Sümen SG, Yakupoğlu S, Gümüş T, Benzonana N. Hyperbaric oxygen treatment for toxic epidermal necrolysis: A case report. Diving and Hyperbaric Medicine. 2021 June 30;51(2):216–219. doi: 10.28920/dhm51.2.216-219. PMID: 34157739.) Toxic epidermal necrolysis (TEN) is a potentially life-threatening muco-cutaneous disease, largely caused by an idiosyncratic reaction to medication or infectious disease, and is characterised by acute necrosis of the epidermis. No definitive consensus regarding the treatment of TEN has been agreed. A 60-year-old woman, diagnosed with multiple myeloma three months prior, was admitted with signs of TEN to the intensive care burns unit. She had been given ciprofloxacin to treat a urinary tract infection. She complained of malaise and pain, with maculopapular and bullous eruptions over her whole body on the third day of ciprofloxacin administration. Her supportive cares included intravenous immunoglobulins, pain control with analgesics, wound care, nutrition, and fluid support. Hyperbaric oxygen treatment (HBOT) was added on the second day of admission. The patient underwent 5 sessions of HBOT at 243.1 kPa (2.4 atmospheres absolute). Desquamation was noted to stop after the first session of HBOT and re-epithelisation commenced rapidly. The patient was discharged from the burn unit after 14 days of hospital admission. Improvement in this case was temporally related to the initiation of HBOT.

Introduction

Toxic epidermal necrolysis (TEN) is a muco-cutaneous disease, typically caused by idiosyncratic adverse reactions to medication use or from infectious agents.[1] It is characterised by acute necrosis of the epidermis. Although rare (the incidence rate is 0.5–1.4 per million per year), the condition of the patient is usually characterised by a rapid deterioration in clinical state due to the systemic effects of the disease.[1] As a consequence of this rapid deterioration in clinical status, the mortality rate may be up to 40% despite the application of multiple treatments tailored for the disease.[1–3]

Patients typically present with symptoms of fever, sore throat, myalgia, coupled with the cutaneous findings, such as macular erythematous eruptions, bullae or necrosis of the skin.[4] The current treatment modalities consist of intravenous immunoglobulin, pain control with analgesics, wound care, nutrition and fluid support, and anti-infective therapy tailored in accordance with the signs and symptoms of the patient.[5,6] A patient is reported who had an acute skin eruption diagnosed as TEN and who underwent emergency hyperbaric oxygen treatment (HBOT) which was temporally associated with onset of improvement.

Case report

Written consent was obtained from the patient to publish this account of her case and photographs.

The patient was a 60-year-old woman with a medical history of chronic renal failure, hypertension and multiple myeloma, the latter diagnosed three months earlier. Due to difficulties in accessing the patient's medical records at another hospital, the details of treatment of the multiple myeloma could not be obtained. However, the patient had been administered vancomycin and gentamicin therapy after being diagnosed with acute bacterial endocarditis. Vancomycin was stopped on the 25th day of therapy because of a diffuse

Figure 1
Upper body skin appearance on admission, prior to HBOT

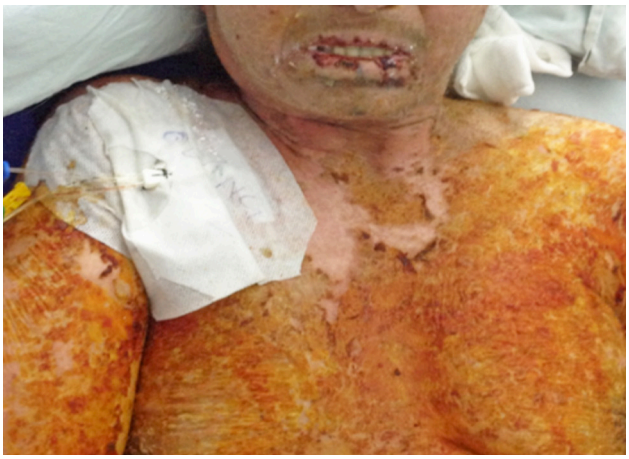
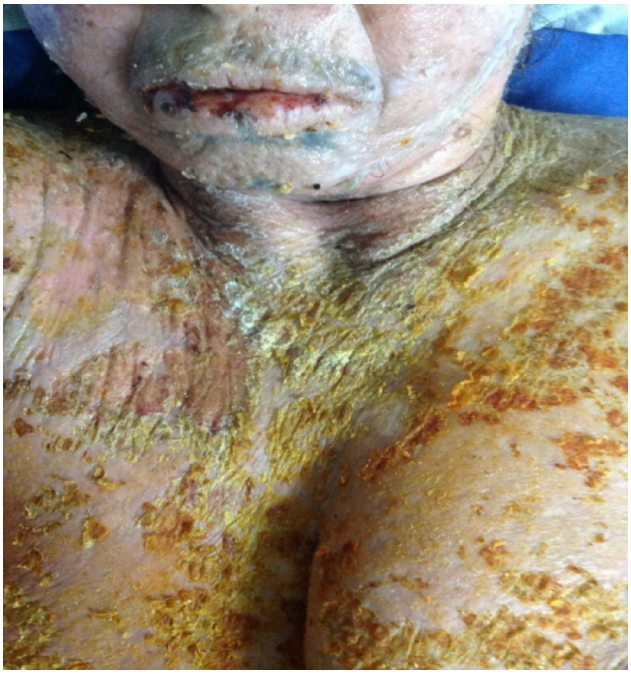


Figure 2
Upper body after completion of HBOT showing regression of skin eruptions



maculopapular rash attributed to vancomycin allergy. She was then transferred to a tertiary facility for autologous haematopoietic stem cell transplantation. Ciprofloxacin (400 mg orally once daily) was started because of urinary tract infection spotted by chance in addition to the acute bacterial endocarditis. The next day, cutaneous lesions together with erythematous maculopapular eruptions with desquamations were observed on her lips, face, head, neck, and arms. On the third day of the antimicrobial therapy, she experienced fever, malaise, and pain, with maculopapular eruption over the whole body. The administration of ciprofloxacin was halted due to the extensive skin eruption, facial swelling and oedema of upper and lower limbs. Purulent secretions and hyperaemia were observed in her conjunctivae, bullous lesions appeared, and desquamation started on the fifth day of admission. She was referred to a dermatology inpatient ward, where she was treated with intravenous immunoglobulin. Her general medical condition deteriorated, and the patient was transferred to the burns intensive care unit.

On her admission to the hospital, she was found to be afebrile with basal temperature of 36.2°C, a pulse rate of 90 beats per minute, and elevated systolic blood pressure at 164/79 mmHg. Her body, including her eyelids, was oedematous and there were bullous maculopapular eruptions (Figure 1). A gentle pressure on the skin caused detachment of epidermis from dermis (known as a positive Nikolsky sign).[4] Furthermore, her conjunctivae were hyperaemic, and her lips were covered with haemorrhagic and erosive lesions with crusts. Eighty percent of her body surface area was affected. The prognosis was evaluated via a severity-of-illness score specifically developed for TEN (SCORTEN). This validated assessment tool is typically used worldwide and based on seven clinical and laboratory findings. The mortality rate increases from 3.2 % with a score of 0–1 to 90% with a score of ≥ 5.[4] The SCORTEN score was calculated as 5 and predicted mortality risk was estimated to be 90%. Laboratory evaluation of her blood sample showed: leucopenia (white blood cell count 2.15 x $10^{9}\cdot L^{-1}$, reference range 4.5–10 x $10.0^{9}\cdot L^{-1}$); anaemia (red blood cell count 2.59 x $10^{12}\cdot L^{-1}$, reference range 3.5–5.5 x $10^{12}\cdot L^{-1}$); haemoglobin: 7.6 $g\cdot dL^{-1}$; haematocrit: 23.2%.

Moreover, *Klebsiella pneumoniae* and *Acinetobacter baumanii* were cultured from her blood taken on the first and fourth days of admission respectively. Based upon the sensitivities of the isolates from the blood cultures, the patient was treated with meropenem and colistin for fourteen days. Subsequent to this two-week intravenous antimicrobial treatment, repeat blood cultures of the patient were negative on the day of discharge from the burn care unit. Symptomatic treatment included pain control with opioid analgesics, wound management, prevention of stress ulcers, nutrition, and fluid support. As a consequence of widespread lesions on the skin and difficulty in wound healing, HBOT was also added to her medical treatment on the second day of admission. The patient underwent five sessions of HBOT applied at 243.1 kPa for 120 minutes per session in a multiplace chamber. Epidermal detachment was noted to stop within 24 hours of commencing HBOT and re-epithelisation started rapidly. The general condition of the patient improved daily and the rash subsided (Figure 2). The patient was transferred out of intensive care to a general ward after 14 days once her clinical status improved.

Discussion

TEN is most often a drug or infectious agent-mediated disease process that presents with signs ranging from erythema multiforme, bullous detachment to necrosis of the skin. It has been described with 220 medications, but only particular drugs are strongly associated with the occurrence of the disease.[3,4,7] The term toxic epidermal necrolysis was defined by scientist Alan Lyell in the 1950's.[8] The incidence rate in clinical studies is 0.5–1.4 cases per million per year. Men are less affected than women with a ratio of 1:1.5.[4] The development of TEN following administration of certain antimicrobial drugs, especially fluoroquinolones (ciprofloxacin, ofloxacin, levofloxacin, norfloxacin) is widely reported.[9–13] The patient reported here was also treated with a fluoroquinolone before admission. Although the skin rashes appeared after administration of ciprofloxacin, it is difficult be certain which drug precipitated the TEN reaction. Underlying malignancy such as multiple myeloma or other medications may be considered to contribute to the presentation of the disease.

Patients usually present with constitutional symptoms such as fever, sore throat, cough, myalgia, and malaise on the first three days of disease. In addition to systemic symptoms, the cutaneous findings initially present as erythematous eruptions, purpura or bullae and frequently disseminate all over the body.[4,7] These lesions exhibit Nikolsky's sign which is defined as separation of epidermis triggered by slight pressure on the skin surface.[14] The disease has a high morbidity and mortality rate associated with being susceptible to secondary super-infection.[15]

TEN patients are usually treated in either intensive care units or burns units at hospitals. The essential treatment of TEN necessitates prompt diagnosis and withdrawal of causative medications. Patients with TEN are provided with supportive care consisting of isolation, fluid and electrolyte replacement, regulation of acid-base imbalance, nutrition support, analgesia, prophylaxis of deep vein thrombosis, prevention of pressure ulcers and infection, and appropriate wound management.[16] HBOT has been widely used in the treatment of various wound types, and was applied here as an adjunct to supportive care. Potential contributions to benefit include antimicrobial effect, reversal of tissue hypoxia, reduction of tissue oedema, enhancement of immune function, and acceleration of epithelialisation.[17,18] After five HBOT sessions, re-epithelialisation was apparent. Our literature review revealed only one similar case report in which three patients with drug-induced TEN were treated with HBOT. It was concluded that patients were successfully treated by means of HBOT after applying approximately 10 treatments.[19]

The mortality rate of TEN is high, and although there are several supportive treatment options, HBOT as an early adjunct to standard supportive care may reduce both morbidity and mortality and enable shorter hospitalisation.

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