Biological skin substitutes to treat toxic epidermal necrolysis in a case with human immunodeficiency virus infection

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Toxic epidermal necrolysis (TEN) is a rare, but life-threatening medical emergency with significant morbidity and mortality. Current treatment standards for TEN patients include stopping all possible drugs associated with the new onset of symptoms, prompt referral and treatment in a specialized center with fluid resuscitation, adequate analgesia and maintenance of nutritional needs. Extensive debridement of the involved epidermis followed by coverage with a skin substitute reduces the mortality from a skin infection and also improves the fluid and electrolyte balance and pain control. This is increasingly considered an important part of the intensive care of these patients. Admitting physicians should be aware of this rare but life-threatening emergency, to allow prompt diagnosis and avoid delays in treatment.

Key words: Human immunodeficiency virus, toxic epidermal necrolysis

INTRODUCTION

Toxic epidermal necrolysis (TEN) is a rare, life-threatening medical emergency in which there is extensive epidermal sloughing and mucositis.[1] It is caused by a variety of different drugs (most commonly sulfonamides, non-steroidal anti-inflammatory drugs, anti-malarials, anticonvulsants and allopurinol).[2] The mortality in TEN varies between 30% and 50%.[3,4] Early recognition allows prompt treatment and an immediate transfer to a burns unit or a specialized intensive care setting and better potential for successful recovery.

CASE REPORT

A 31-year-old Caucasian male with a recent diagnosis of human-immunodeficiency virus (HIV) was started on co-trimoxazole, 960 mg twice daily for Pneumocystis carinii prophylaxis. He had no HIV-related symptoms. He noticed a rash appearing on his hands 5 days after starting the treatment; however, he continued taking the co-trimoxazole. He presented to his genito-urinary medicine clinic 7 days later with fever, skin pain, malaise, myalgia and an extensive erythematous rash, which covered the trunk and limbs; he was sent promptly to the medical assessment unit. He was pyrexial, tachycardic, normotensive and in pain. A tender pink macular rash covered the majority of the surface of his limbs and trunk, with extensive bullous areas of epidermal sloughing. The palms and soles were also affected. There was also a diffuse mucosal ulceration of the mouth and the oropharynx [Figures 1-4]. The admission bloods and the chest X-ray did not reveal any abnormality. The Score for TEN (SCORTEN) score,[5] on admission was two, with patient scoring for tachycardia and having a detached body surface area of >10%.

The offending drug was stopped and the patient was commenced on IV fluids, morphine analgesia and antibiotics. An urgent dermatology opinion the same evening confirmed the proposed diagnosis of TEN secondary to co-trimoxazole. Patient was immediately transferred to a burns unit. Fluid and electrolyte balance was carefully monitored and he was given high calorie enteral feeds. Extensive debridement of the involved epidermis was followed by grafting with an artificial skin substitute called “Biobrane.”[6]

Patient had the skin substitute placed on his trunk and limbs, covering a body surface area of approximately 22%. Post-operatively the outer dressings were changed daily. The skin substitute stayed on for the next 2 weeks after which it was removed once the skin had healed.

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DISCUSSION

TEN is a life-threatening idiosyncratic drug reaction. It is important to recognize TEN as it requires prompt treatment and immediate transfer to a burns unit or a specialized intensive care setting. The mortality of TEN varies between 30% and 50%, with the primary cause of death being infection and multi-system organ failure. The risk of developing TEN is 1000 times higher in patients with HIV and acquired immune deficiency syndrome than in the normal population. Therefore, in a patient with known HIV and new onset of an erythematous bullous rash after commencing a new treatment, it is important to include TEN as a differential.

SCORTEN is a severity-of illness score with which the severity of TEN can be assessed by looking at seven independent risk factors. A high score indicates a higher rate of mortality for the patient. Patient is scored on age, associated malignancy, heart rate, serum urea, detached body surface area, serum bicarbonate and serum glucose.

The clinical features typically associated with TEN include a prodrome of 2-3 days characterized by fever, cough, sore throat, severe skin pain and general malaise which is then followed by an acute macular rash. There is a rapidly spreading necrosis of the mucus membranes, which is then followed by similar events in the epidermis. Nikolsky sign, which is characterized by epidermal separation induced by gentle lateral pressure on the skin surface is usually present. Mucus membranes, including conjunctival, pharyngeal, tracheal and esophageal, are also usually affected.

As the cutaneous injury in TEN is similar to a partial skin thickness burn, the patient should be admitted to a burns unit, where meticulous wound care can be provided. The triggering drug should be immediately discontinued as this reduces mortality and improves prognosis. An urgent review by the dermatologist on call will usually allow a confident clinical diagnosis. Otherwise, biopsies of the skin or the bulla roof for immediate frozen histological sections can promptly differentiate between TEN and staphylococcal scalded skin syndrome. At the time of admission a burn diagram should be used to plot the area of skin sloughing. It is important to ensure good pain relief and a patient controlled analgesia pump may be useful. If large areas of necrotic tissue are present, sharp debridement in the
operating room under anesthesia should be carried out. Risks of wound infection and sepsis are minimized by good wound care. Wet dressings maintain a moist wound environment, speed re-epithelialization, minimize pain and decrease infection rates.[1,10]

Biobrane is a biosynthetic semi-permeable membrane designed to temporarily perform the functions of lost epidermis until re-epithelialization occurs. It is a bi-layer material where the silicone outer layer acts like a protective epidermal barrier and the inner surface is composed of a three dimensional interwoven nylon filament structure upon which collagen peptides are boarded.[6] The material bonds firmly to the adequately prepared bed of an appropriate burn (superficial partial thickness to mid-dermal injury) until spontaneous detachment by re-epithelialization.[11]

In the management of TEN the benefits of high-dose corticosteroids and/or high-dose immunoglobulin infusions within 48-72h of onset of bulla formation remain unconfirmed. As blister fluid is rich in pro-inflammatory factors such as interleukins and the blister roof is necrotic, coverage with artificial skin substitutes such as Biobrane provide optimal protection until the epidermis completely regenerates.[4,12] This also minimizes wound infections and prevents scarring during the healing. The use of such dressings on exposed dermis and the sensitive dermal nerve endings avoids frequent dressing change and minimizes pain and discomfort.[4,10]

**CONCLUSION**

TEN is a life-threatening medical emergency. The risk of developing TEN is a 1000 time higher in a HIV positive patient. Prompt diagnosis of TEN avoids a delay in treatment and allows a speedy transfer to a burns unit, where fluid resuscitation, adequate analgesia and meticulous wound care can be provided. The use of artificial skin substitute can reduce the risk of wound infection, sepsis, improve pain control and provide protection until the epidermis regenerates.

**REFERENCES**


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