

Toxic Epidermal Necrolysis: A Case Report in Azal hospital, Sana'a, Yemen

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Abstract

Toxic epidermal necrosis (TEN) is a life-threatening connective tissue disorder also known as Lyell's syndrome, characterized by erythema, and epidermal detachment, manifests as blisters, and raw skin patches. Adverse drug reactions are the most common risk factors. TEN is identical with Steven-Johnson's syndrome (SJS), differs from the latter in that greater area of the skin is involved. In this article, we report a case of a 20 years old male patient who presented with complaints of lethargy, red eyes and blisters after prescription of carbamazepine. Following this, the drug was taken off immediately. The treatment included the administration of fluids and appropriate antibiotics for treating the fluid-filled vesicles. The treatment regimen continued for three weeks and was stopped when the skin lesions were minimal and there was an improvement in the overall health of the patient.

Keywords: toxic epidermal necrolysis (TEN), Stevens-Johnson's syndrome (SJS), drug reaction, carbamazepine.

Conflict of interest statement

The authors declare no conflict of interest.

Introduction

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are life-threatening diseases characterized by detachment of the epidermis and mucous membrane. SJS/TEN are considered to be on the same spectrum of diseases with different severities. They are classified by the percentage of skin detachment area. SJS/TEN can also cause several complications in the liver, kidneys, and respiratory tract. The pathogenesis of SJS/TEN is still unclear. Although it is difficult to diagnose early stage SJS/TEN, biomarkers for diagnosis or severity prediction have not been well established. Furthermore, optimal therapeutic options for SJS/TEN are still controversial. Several drugs, such as carbamazepine and allopurinol, are reported to have a strong. Skin detachment in SJS/TEN skin lesions is caused by extensive epidermal death, which has been considered to be apoptosis via the Fas-FasL pathway or perforin/granzyme pathway. Necroptosis, i.e. programmed necrosis, also contributes to epidermal cell death. Supportive care is recommended for the treatment of SJS/TEN. However, optimal therapeutic options such as systemic corticosteroids, intravenous immunoglobulin, cyclosporine, and TNF- α antagonists are still controversial (1). TEN is also known as Lyell's syndrome (2). Toxic epidermal necrolysis (TEN) is an immune mediated, severe cutaneous adverse drug reaction characterized by epidermal detachment affecting greater than 30% body surface area. The mortality rate of TEN exceeds 20% and is usually caused by infection and respiratory compromise. Withdrawal of the causative drug, supportive care, and adjuvant therapy improve prognosis (3). Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are rare diseases that are characterized by widespread epidermal necrosis and sloughing of skin. They are associated with significant morbidity and mortality, and early diagnosis and treatment is critical in achieving favorable outcomes for patients (4). Because the pathogenesis has not yet been established, the management and systemic treatment of these syndromes have not been standardised. The efficacy of the treatment options suggested has not been confirmed by clinical studies involving suitably large groups of patients, especially children (5). The pathogenesis of SJS/TEN remains unclear and effective therapeutic agents have not yet been established. As the involvement of innate immunity, such as monocytes and neutrophils, in addition to T cells, has become clear, a more complex pathogenesis is

predicted. Further elucidation of the pathogenesis of SJS/TEN is expected to lead to the development of new diagnostic and therapeutic agents (6). TEN may be associated with other autoimmune diseases for example systemic lupus erythematosus (SLE). Occasionally, acute cutaneous manifestations of SLE and SJS/TEN can be phenotypically similar, both causing extensive epidermal necrosis (7). Toxic erythema of chemotherapy for example of docetaxel is an umbrella term encompassing a range of reactions characterized by symmetric erythematous to dusky presenting with prominent mucosal and periorificial involvement, along with epidermal necrosis, closely mimicking toxic epidermal necrolysis (8). Many dermatoses can present with a TEN-like eruption. Those "TEN-mimics" are a true diagnostic challenge and an alarming differential diagnosis to such a serious condition (9). TEN also has respiratory complications; treatment of these complications may include intubation, tracheostomy, nasoendoscopy, bronchoscopy, ventilation and management of chronic respiratory complications (10).

Case presentation

A 20 years old male soldier entered the emergency unit in our hospital complaining of lethargy, red eyes and generalised skin and mucous membrane blisters including his eyes and oral and nasal mucosa as shown in figures 1 and 2.



Figure 1: The skin and mucous membrane manifestations suspected to carbamazepine



Figure 2: The skin manifestations suspected to carbamazepine

He is unknown case of any medical illnesses, and like most male Yemenis, he chews Khat daily afternoon for about 4 hours. The remarkable note in his history is that he has wounded in his head where he later developed seizures. His neurosurgeon prescribed carbamazepine to treat the seizures. The latter is thought to be the risk factor for his complaints. The suspected medicine, carbamazepine, was withdrawn. The patient is then admitted to an isolated area in the intensive care unit (ICU) where he received the following medications as part of his initial treatment: Ringer's lactate 120 ml per hour, intramuscular injection chlorpheniramine 4 mg twice daily, intravenous dexamethasone 8 mg thrice a day and antibiotic cover: imipenem/cilastatin and vancomycin. The second day, dexamethasone is stopped and the patient received intravenous methylprednisolone 500 mg daily for three days'. After that, the patient received intravenous immunoglobulin 0.5 gram/kg/day for five days. On admission, his vital signs were normal as well as complete blood count, random blood sugar, bicarbonate, renal and hepatic function tests were all within normal. The random blood sugar level was 140 mg/dl. The abnormal parameters were Monocytes 15.9 and albumin 29. As the mucous membrane complications progress, the patient had difficulty in breathing and swallowing. According to the The SCORTEN disease severity score for TEN, the mortality rate for our patient is 2 (11). For his skin lesions the patient is treated by normal saline and fusidic acid, all are topically twice daily. During his stay herpes simplex virus infection is diagnosed, where he received acyclovir 200 mg twice daily. For his eyes, the patient received topical tobramycin/dexamethasone, moxifloxacin and Hyfresh: sodium hyaluronate, moreover, he received gentian violet and mycostatin suspension for his mouth ulcers. After fifteen days, the lesions largely healed and the patient's overall health improved.



Figure 3: After 2 weeks, clear improvement in facial and skin lesions



Figure 4: After 3 weeks, almost total healing in facial and skin lesions

Discussion

Carbamazepine is assumed as the main cause of SJS/TEN in most cases (12, 13, 14). Nearly 1 to 2 patients per 1,000,000 populations are affected annually with SJS and TEN, and sometimes these maladies can cause serious life-threatening events. The reported death rates for SJS range from 1 to 5%, and 25 to 35% for TEN (15). **Fortunately, our patient is young with no comorbidities; the majority of his medical parameters were within normal on admission. However, skin and mucous membranes were severely and extensively affected, with involvement of eyes and oral and nasal mucosa. We succeeded to make an early diagnosis. We recognized that withdrawal of the causative drug, supportive care, and adjuvant therapy is crucial for improved prognosis (16). Fluids were commenced: ringer lactate, antibiotic cover, and dressing and sterilization for topical lesions. Normal saline and fusidic acid ointment were used for skin lesions. Special care was directed to his eyes, with the administration of antibacterial ophthalmological drops and sodium hyaluronate. The second day we started intravenous immunoglobulin 0.5 gram/kg/day for five days. Intravenous immunoglobulin (IVIG) has been proposed as a treatment for toxic epidermal necrolysis (TEN) and Stevens-Johnson Syndrome (SJS) (17). Intravenous methylprednisolone pulse therapy was also commenced in an attempt to speed healing and to improve prognosis (18). During his stay in the ICU we monitor renal and hepatic functions as well as electrolytes and albumin levels. Univariate analysis revealed nine prognostic factors related to death, i.e., age, malignancy, chronic kidney disease (CKD), coronary artery disease, heart rate >120 beats/min, diagnoses of SJS-TEN overlap and TEN, blood urea nitrogen (BUN) >10 mmol/L, hemoglobin <10 g/dL, and serum albumin <2 g/dL (19). After 15 days we evaluate the patient, he is haemodynamic stable, with almost near complete healing of his skin lesions, his vision is preserved. According to past research, systemic steroids, antibiotics, and adjunct therapies were used to treat the majority of TEN patients [20, 21]. Just before patient transferred**

from the ICU, we checked the immune markers: antinuclear antibody (ANA) and anti-double-stranded (ds) DNA, both were within normal. Acute cutaneous manifestations of systemic lupus erythematosus (SLE) and SJS/TEN can be phenotypically similar, both causing extensive epidermal necrosis. SJS/TEN has a very high mortality, but is rare, and cases of SJS/TEN combined with systemic lupus erythematosus (SLE) are even less common (22).

Conclusion

Toxic epidermal necrolysis is a highly dangerous medical emergency and should be diagnosed early for good prognosis. Intravenous fluids, skin and mucous membranes dressing, and sterilization are the cardinal treatment in this case. Specific pharmacological treatment such as corticosteroids and intravenous immunoglobulins are still controversial. The authors **feel that these pharmacological interventions used in their patient contribute to his healing and prognosis.**

Human Ethic

Consent was obtained or waived by all participants in this study.

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النخر البشري السُمي، تقرير حالة في مستشفى آزال، صنعاء، اليمن

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الملخص:

النخر البشري السُمي هو مرض من أمراض النسيج الرابط يهدد حياة المريض و يُعرف بمتلازمة Lyell. و يتميز هذا المرض بالطفح الحمامي و انسلاخ الجلد و ظهور نطف جلدي و يقع منزوعة الجلد. و يحدث غالباً كعرض جانبي غير متوقع لبعض الأدوية. النخر البشري السُمي مطابق تماماً لمتلازمة Steven-Johnson، و يختلف عنها بزيادة المساحة الجلدية المصابة. في هذه الورقة البحثية وثقنا حال مريض عمره عشرون عاماً حضر و هو يعاني من فتور و احمرار العينين و ظهور نطف جلدي سطحي بعد استخدام عقار ال carbamazepine. تم إيقاف العقار حالاً و بدأنا خطة المعالجة و التي شملت إعطاء المريض السوائل الوريدية و المضادات الحيوية المناسبة لعلاج النطف الجلدي الممتلئ بالسوائل. و استمرت المعالجة لمدة ثلاثة أسابيع حتى تحسنت الآفات الجلدية و تماثل المريض للشفاء.