

CASE REPORT

Clindamycin induced toxic epidermal necrolysis versus Staphylococcal scalded skin syndrome: a case report

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Abstract

Toxic epidermal necrolysis and Staphylococcal scalded skin syndrome (SSSS) are potentially life-threatening dermatological emergencies that present in a similar clinical fashion. Toxic epidermal necrolysis is typically triggered by anticonvulsant and other neurological medications and reports clindamycin inducing the disease is exceedingly rare. SSSS seldomly occurs in adult patients. We present the case of a 60-year-old male presenting with dermatological rash covering >80% his body surface. Diagnosis and therapy involved multidisciplinary contribution from medical physicians, dermatologists, microbiologists and histopathologists to provide a favourable outcome.

INTRODUCTION

Toxic epidermal necrolysis (TEN) and Staphylococcal scalded skin syndrome (SSSS) have the tendency to mimic one another on clinical presentation in the form of a widespread, blistering Nikolsky positive rash. Differentiation and accurate diagnosis of both diseases depend upon thorough clinical examination with subsequent comprehensive histological reporting. Lincosamide antibiotics such as clindamycin have rarely been associated with TEN in medical literature and medications such as anticonvulsant and antipsychotics being recognised as the major pharmacological triggers of the disease [1]. Similar to TEN, adult SSSS is a disease known to carry a high mortality rate with poor predictability of outcome when compared to the paediatric population who suffer from the disease [2, 3]. The purpose of this case report is to report a diagnostic conundrum of clindamycin induced TEN vs SSSS

in a 63-year-old male patient who presented to the emergency department of a University Teaching Hospital in the West of Ireland late in August 2019. This report outlines factors in differentiating these two dermatological emergencies and the difficulties faced in treating such a case on presentation to the emergency department.

CASE PRESENTATION

A 63-year-old male presented with a 2-day history of a widespread, erythematous rash covering all surfaces of his body. The rash appeared 2 days prior to admission with associated prodromal malaise and anorexia. His medical history was significant for a cellulitis of his left lower limb for which he was prescribed oral clindamycin 5 days prior. Two days before admission, the patient noted a pruritic rash on his abdomen

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Figure 1: Image demonstrating the oatmeal dermatitis affecting the patients oral and nasal facial mucosa.



Figure 2: Sparring of the mucosal membranes of the oatmeal dermatological rash.

which subsequently became erythematous. The rash then migrated to his face and the rest of his torso. Within the next 48 h, it spread to involve his back and upper and lower limbs. The patient then began experiencing subjective fever and presented to his general practitioner before being referred to hospital. On hospital presentation he was afebrile, tachycardic (irregularly irregular pulse rate of 170 beats per min) and was tachypnoeic (respiratory rate of 28). He was normotensive (126/84 mmHg) and remained alert and interactive. Clinical examination was remarkable for an oatmeal dermatitis of the face and perioral area (Figs 1 and 2) and an erythematous, blistering rash covering 80% of his total body surface area. Nikolsky sign was positive. Oral involvement was noted. The palms of his hands and the soles of his feet were spared.

Potentially causative medications (including clindamycin) were stopped. Electrocardiogram confirmed atrial fibrillation. The patient was immediately isolated from other patients and increased contact precautions were taken. Fluid resuscitation was commenced as per local hospital sepsis guidelines and

urinary output monitored. Paraffin gel was applied liberally two hourly and potent topical corticosteroids twice daily. Intravenous hydrocortisone (100 mg) was given four times daily. Laboratory investigations on admission were significant for a moderate leucocytosis of $15.5 \times 10^9/l$ and a neutrophilia of $14.5 \times 10^9/l$. C-reactive protein levels were 123 mg/l and venous lactate was markedly elevated at 6.5 mg/dl. Blood, urine and wound site cultures were sent for culture and sensitivity. Autoimmune and viral screens were taken. Skin biopsies were performed on two occasions: A 4 mm punch biopsy of affected skin was taken from the anterolateral left forearm and a repeat punch biopsy was taken from the sacral area on Day 2 of admission. The patient's chest X-ray revealed no abnormality.

A marked improvement in the patient's rash was seen on admission Days 3 and 4, and his clinical condition gradually improved. The patient remained afebrile. A switch from intravenous hydrocortisone to 30 mg of oral prednisolone was made on Day 7. The patient evidenced impressive regeneration of the affected skin and corticosteroids were tapered prior to discharge 21 days after admission.

DISCUSSION

TEN and SSSS may provide diagnostic dilemma for clinicians on the basis of their similar clinical manifestations. Table 1 illustrates the important clinical and histopathological considerations for accurate diagnosis of these potentially life-threatening diseases at presentation and during workup.

TEN is a potentially life-threatening dermatological emergency carrying a mortality rate of ~26% [4]. Antibiotics, anticonvulsant drugs, and non-steroid antiinflammatory drugs are described in medical literature as common inducers of the Steven-Johnson syndrome-toxic epidermal necrolysis disease spectrum (SJS-TEN) [1, 5]. Lincosamide antibiotics such as clindamycin are poorly recorded as being causative: formal literature review of the PUBMED, SCOPUS and MEDLINE databases results provided only five recorded cases of clindamycin as a putative trigger of SJS/TEN syndromes. These cases typically involved acute onset rash developing over a number of hours post clindamycin administration. All of these cases involved corticosteroid as a primary therapeutic agent and consequential settling of symptoms. Our patient reported a history of clindamycin treatment for leg cellulitis 5 days prior to presentation which raised suspicion for a drug-induced hypersensitivity reaction. Initial histological reporting during patient workup described: 'fragments of detached necrotic epidermis and stratum corneum with parakeratotic changes with no bacterial colonies'. When considering this patient's history and clinical picture in combination with epidermal tissue necrosis as the main histopathological diagnostic feature in TEN, this was considered the working diagnosis for this case.

SSSS is a superficial epidermolysis skin disorder triggered by exfoliative toxins A and B produced by 5% of *Staphylococcus* [6]. This condition, first described by Ritter von Rittershain in 1878, is well described in paediatric patients and carries a mortality of up to 50% [7]. Diagnosis is exceedingly rare in the adult population [2, 8]. Formal diagnosis of SSSS is made when histopathological evaluation demonstrates a subcorneal split along the granular cell layer which contain acantholytic cells, whilst inflammatory cell infiltrate and cell necrosis are characteristically absent [9]. Our patient's epidermal biopsies taken 2 days after his initial biopsy yielded results favouring SSSS as a histopathological diagnosis: '...skin showing a thick surface crust composed of

Table 1: Clinical, pathophysiological and diagnostic differences between TEN and SSSS

	Toxic epidermal necrolysis	SSSS
Clinical presentation	Widespread blistering, positive Nikolsky sign, erythematous, tender skin	Widespread blistering, positive Nikolsky sign, erythematous, tender skin
Differences in clinical presentation	Base of blistering tends to be pink or white (the colour of dermis), while surrounding skin is brown, tan or black due to melanin pigment at and above the basal layer of the epidermis, no mucosal involvement, typically occurs after pharmacological trigger	Base of blistering tends to be the same colour as the surrounding adjacent skin, mucosal involvement, typically paediatric patients and atypically in adults, adult patients usually have renal impairment
Mortality	26% [4]	4–11% in children, 40–63% in adult population [3, 9]
Pathophysiology	Pathophysiological mechanism is largely unknown; usually a pharmacological or infectious trigger are thought to drive a CD8+ cytotoxic lymphocyte delayed hypersensitivity response against an individual's own keratinocytes. A protein called granulysin is released by cytotoxic CD+ lymphocytes and natural killer cells has been identified in in vitro and animal studies as a key molecule underlying development of the characteristic lesions of SJS–TEN	Histologically, epidermal layer is detached, blisters affect subcorneal layer. Epidermal detachment occurs in sheets due to Staphylococcal exotoxin producing a serine protease that destroys desmoglein 1 in the epidermis (handler). Adult patients with renal impairment tend to be affected by SSSS as they fail to excrete exotoxins produced by Staphylococcal bacteria [9]
Histological diagnostic features	Dermal-epidermal blister with focal dyskeratosis and areas of full thickness epidermal necrosis	Subcorneal bullae with scant inflammation

mixed neutrophils and parakeratotic material with possible bacterial colonies present, no evidence of vasculitis, no evidence of bullous change. Provisional conclusion: 'There is no evidence of vasculitis or the histological features of TEN. The histological differential diagnosis would include staphylococcus scalded skin syndrome although no subcorneal bulla is seen'. Patients with SSSS have the classic tendency to have scant inflammatory response on histological tissue biopsy, yet our patient's second biopsy manifested the presence of mixed neutrophils. Despite this, patients may develop leucocytosis on blood film and our patient displayed only moderate leucocytosis despite the severe nature of his rash encompassing 80% of his total body surface area. Clinically, pyrexia would be typically be expected in SSSS; however, our patient remained afebrile throughout his hospital admission. Interestingly, our patient was prescribed clindamycin as a measure to treat cellulitis. It is plausible this cellulitic tissue harboured a *Staphylococcus* infection, which may have possessed the endotoxins necessary to potentiate SSSS. This theory further complicates this diagnostic conundrum. However, repetitive swab cultures from blister sites and blood cultures were negative for *Staphylococcus* infection rendering SSSS diagnosis less likely. These clinical inconsistencies for textbook knowledge of these conditions added complexity diagnosis.

This case demonstrates a favourable outcome despite ambiguity in suspected dermatological disease processes and disparate histology. Staphylococcal scalded skin and toxic epidermal necrolysis are known to clinically present in an almost analogous manner despite disparate disease processes and can pose diagnostic difficulty as clearly outlined in this case where a patient does not clearly fit into either disease process.

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CONFLICT OF INTEREST STATEMENT

None declared.

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ETHICAL APPROVAL

Not applicable.

CONSENT

Verbal and written consent was obtained from this patient.

GUARANTOR

Not applicable.

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