Case Report

Stevens–Johnson syndrome/toxic epidermal necrolysis overlap syndrome due to oral cefuroxime

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Abstract

Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are life-threatening and severe cutaneous adverse drug reactions characterised by epidermal detachment presenting as blisters and differ only by their extent of skin detachment. A 22-year-old male presented to our tertiary care teaching institute with fever for the preceding 5 days and macular rash over the back for the past 1 day. Before this, he had consulted a local physician for fever and was using oral cefuroxime (250 mg bid) for the past 5 days. General physical examination revealed fever (103 °F), conjunctival congestion, generalised maculopapular rash and ulcers over the lips. He was admitted to medical intensive care unit. On the next day, fever persisted; rash had worsened, conjunctivitis developed and skin peeling became evident, involving >10% but <30% of body surface area. At this point in time, a diagnostic possibility of an adverse drug reaction was considered and the patient's history was thoroughly reviewed again. Oral cefuroxime was stopped. Dermatology consultation was sought. Based on clinical presentation, the patient was diagnosed to have SJS/TEN overlap syndrome. He was treated with intravenous linezolid 600 mg twice daily, topical antibiotics and symptomatic management. The patient recovered, skin lesions subsided and he was discharged from the hospital in a stable condition after 2 weeks of in-hospital stay. The present case documents the rare occurrence of SJS/TEN overlap syndrome as an adverse drug reaction with cefuroxime treatment.

Keywords: Cefuroxime, Cutaneous adverse drug reactions, Stevens–Johnson syndrome

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INTRODUCTION

Stevens–Johnson syndrome (SJS) was first described in 1922, as an acute mucocutaneous syndrome. The condition was characterised by severe purulent conjunctivitis, severe stomatitis with extensive mucosal necrosis and purpuric macules.[1] It became known as SJS and was recognised as a severe mucocutaneous disease with a prolonged course and potentially lethal outcome that is often drug induced. In 1956, Alan Lyell described four patients with an eruption resembling scalding of the skin which he called toxic epidermal necrolysis (TEN).[2] Subsequently, it became known that TEN was drug-induced, and drugs such as sulphonamides, pyrazolones, barbiturates and antiepileptics were the most frequent triggers for TEN. At present, SJS and TEN are considered to be two ends of a spectrum of severe epidermolytic adverse cutaneous drug reactions, differing only by their extent of skin detachment.[3] Cephalosporins are widely used to prevent infections in

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outpatients with genitourinary tract, upper respiratory tract and skin infections and in patients undergoing surgery. SJS is rare with oral cefuroxime. Here, we report a rare presentation of SJS-TEN overlap syndrome caused by oral cefuroxime.

CASE REPORT

A 22-year-old male presented with fever for preceding 5 days and macular rash over the back since 1 day. Before this, he had consulted a local physician for fever and he was using oral cefuroxime 250 mg bid for the past 5 days. General physical examination revealed that he was febrile (temperature: 103 °F), pulse: 110/min, respirations: 28/min, blood pressure: 100/70 mmHg and oxygen saturation (measured by pulse oximetry) while he was breathing room air was 98%. Conjunctival congestion was evident. A generalised maculopapular rash was present over the anterior aspect of the trunk [Figure 1a]. Rest of systemic examination was unremarkable.

At this point in time, a diagnostic possibility of an adverse drug reaction was considered and the patient's history was thoroughly reviewed again. Oral cefuroxime was stopped. On the 2nd day of admission, fever persisted (temperature 103 °F), rash had worsened, extending over the posterior aspect of the trunk, and few bullae became evident [Figure 1b]. Conjunctivitis developed and adhesions of the eyelids [Figure 2a] were also observed. On the 3rd day of admission, rash further progressed and was evident affecting the face and mid-thighs and genitalia was evident, involving >10% but <30% of body surface area.[4] Skin peeling became evident, and Nikolsky's sign was positive [Figure 2b].

Based on clinical presentation, the patient was diagnosed to have SJS/TEN overlap syndrome.[4] Dermatology consultation was taken. He was started on intravenous (IV) linezolid 600 mg twice daily, topical antibiotics and symptomatic management. Dexamethasone was administered at 8 mg IV tid for the initial 3 days; as the clinical condition was deteriorating, new bullae were appearing, Nikolsky's sign became positive and the dosage of dexamethasone was doubled (16 mg IV, thrice daily) for a further 2 days. As the patient's general condition improved, dexamethasone was stopped.

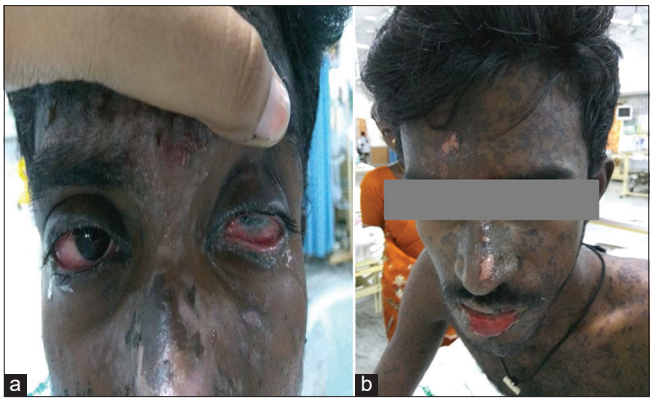

Figure 2: Clinical photograph showing bilateral conjunctivitis with adhesions between eyelid and cornea in the left eye (a); areas of skin denude on the face with red oozing dermis and haemorrhagic crusting of the lips (b)

Ophthalmology consultation was sought. To prevent eyelid symblepharon, topical lacryl gel ointment and moxifloxacin eye drops were administered four times a day; periodic regular sweeping of both the eyelids was done. In spite of the above measures, the patient developed adhesions and pseudomembrane formation between cornea and eyelids. Adhesiolysis was done using paracaine gel.

The patient gradually improved and recovered [Figure 3a and b] and was discharged from the hospital in a stable condition after 2 weeks of in-hospital stay.

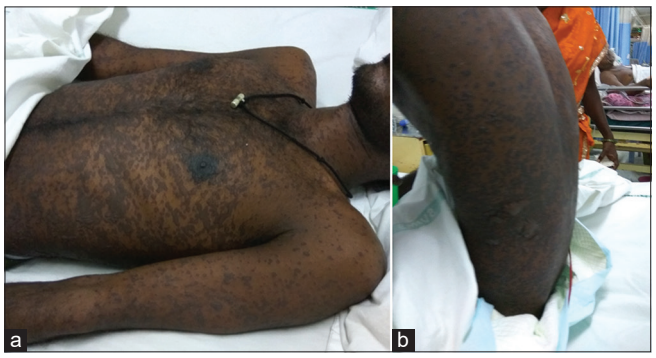

Figure 1: Clinical photograph showing generalised maculopapular rash over the anterior aspect of trunk (a) and over the posterior aspect of the trunk with bullae (b)

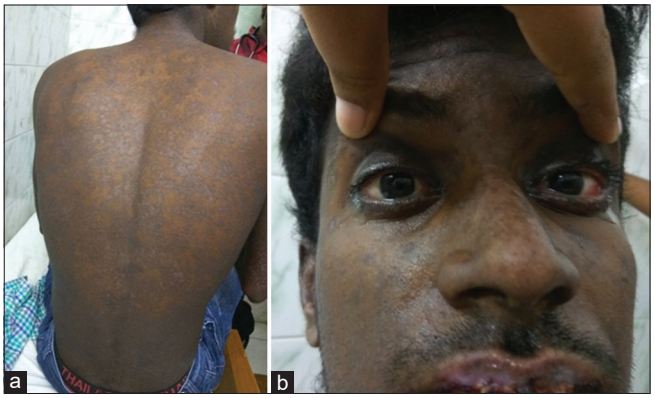

Figure 3: Clinical photograph showing fading lesions over the trunk (a) and cleared conjunctivitis and adhesion in the right eye (b)

DISCUSSION

SJS/TEN are considered as a spectrum of the same disease. When the extent of skin involvement is <10% of body surface area, the condition is termed as SJS. TEN is a more severe condition where skin involvement of >30% of body surface area is seen. When the skin involvement is 10%–30%, it is designated SJS/TEN overlap syndrome.[4] While evaluating the extent of skin involvement, only necrotic skin, which is already detached (e.g., blisters and erosions) or detachable skin (Nikolsky's sign positive), is considered diagnostic.[3,4] In our patient, as the cutaneous involvement was >10% but <30% of body surface area, SJS/TEN overlap syndrome was diagnosed.[4]

SJS and TEN can occur at any age and drugs are considered to be the triggers for SJS and TEN in children as well as in adults. In children, infections are also a common cause of SJS and TEN. In a study,[5] among drugs used for a short-term period, the highest risk of developing SJS or TEN was documented for trimethoprim-sulphamethoxazole and other sulphonamide antibiotics, chlormezanone, cephalosporins, fluoroquinolones and aminopenicillins. Among long-term use drugs, SJS and TEN occurred most frequently during the first 2 months of treatment, and commonly implicated drugs were carbamazepine, followed by oxicam non-steroidal anti-inflammatory drugs, phenytoin, allopurinol, phenobarbital and valproic acid, among others.[5] Our case documents the relatively uncommon occurrence of SJS/TEN syndrome.

In the acute phase of TEN and SJS, symptoms can be non-specific and include fever, stinging sensation in the eyes and discomfort upon swallowing. Typically, these symptoms precede cutaneous manifestations by a few days. Cutaneous involvement of the presternal region of the trunk and the face and also the palms and soles occurs early. Erythema that is often confluent and erosions of the buccal, ocular and/or genital mucosa occurs in >90% of patients; in some cases, the respiratory and gastrointestinal tracts are also affected.[5] Large areas of epidermal detachment develop. In the absence of epidermal detachment, more detailed skin examination should be performed by exerting tangential mechanical pressure on several erythematous zones and watching for epidermal detachment (Nikolsky's sign). The extent of skin involvement is a major prognostic factor in patients with SJS and TEN.[4] Ocular involvement at the onset of disease is frequent and can range from acute conjunctivitis, eyelid oedema, erythema, crusts and ocular discharge to conjunctival membrane or pseudomembrane formation or corneal erosion. In severe cases, cicatrising lesions, symblepharon, fornix foreshortening and corneal ulceration are described.[6] The clinical presentation of our patient was similar.

Differential diagnoses include autoimmune blistering diseases, bullous fixed-drug eruptions, acute generalised exanthematous pustulosis and staphylococcal scalded skin syndrome (which is rare in adults), among others. Histopathological examination including direct immunofluorescence analysis of the skin biopsy can help, but histopathological findings are neither specific nor considered diagnostic.

There are no universally effective and established therapies for SJS/TEN other than supportive care. The treatment of SJS/TEN includes early identification and withdrawal of the offending trigger, symptomatic and supportive management. Adjunctive therapies such as glucocorticoids and IV immunoglobulin have been tried with varying results, and no data from randomised controlled trials are available establishing their efficacy. Further, there is no consensus on the optimal dosage for corticosteroid use in this condition with a wide dosages being used.[7] As our patient had rapid clinical deterioration, progression of lesions and occurrence of Nikolsky's sign, we had used IV dexamethasone for a short duration.

Our case documents a rare presentation of SJS-TEN overlap syndrome with oral cefuroxime. Early diagnosis with the prompt recognition and withdrawal of all potential causative drugs is essential for a favourable outcome.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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