

Aceclofenac induced Stevens-Johnson/toxic epidermal necrolysis overlap syndrome

Kaderthambi Hajamohideen Nooru Ameen, Rakesh Pinninti, Swathi Jami

Department of General Medicine, Government Stanley Hospital, Chennai, Tamil Nadu, India

ABSTRACT

The purpose of this paper is to report a rare occurrence of Stevens-Johnson/Toxic epidermal necrolysis (SJS/TEN) overlap syndrome after the use of aceclofenac. A 38 year old healthy adult male presented with rapidly evolving rash over face and upper body with ulceration of buccal mucosa and breathlessness after taking aceclofenac tablet. Naranjo score for this adverse drug event was six, thereby making it a probable adverse drug reaction. Despite aggressive fluid resuscitation and use of antihistamines and systemic steroids, patient's health rapidly worsened and died within six hours of presentation. Aceclofenac induced SJS/TEN overlap is an extremely rare clinical association previously reported only once in medical literature. To the best of our knowledge, this is the first case report of such an association in the Indian population. We are presenting this case to highlight the serious adverse reactions possible from a routinely prescribed drug.

Key words: Corticosteroids, Stevens-Johnson syndrome, toxic epidermal necrolysis

INTRODUCTION

Aceclofenac is an orally administered non-steroidal anti-inflammatory drug commonly prescribed for relief of pain and inflammation in rheumatologic disorders. The mode of action of aceclofenac is largely based on the inhibition of prostaglandin synthesis. Aceclofenac is a potent inhibitor of the enzyme cyclooxygenase, which is involved in the production of prostaglandins. Aceclofenac is well tolerated, with most adverse events being minor and reversible and affecting mainly the GI system. Other adverse effects are dizziness, vertigo, paraesthesia and tremor. Here, we report a case of aceclofenac induced SJS/TEN overlap syndrome,

a clinical association that is not previously reported from Indian population.

CASE REPORT

A 38 year old male presented to our toxicology department with complaints of rapidly evolving rash over his face, upper torso and hands, he also had breathlessness. Patient gives history of taking analgesics (aceclofenac 100 mg one tablet) obtained over the counter for backache around 11 am on the day before presentation, later in the evening around 9 pm he noticed a rash over his lips and cheeks as erythematous macules and clear fluid filled vesicles. He also had itching and burning around the lips and eyes. Patient complaints were self-limited and he failed to seek medical help. Patient took another tablet for headache before resuming to bed (around 11 pm). Around 1 am patient noticed that rash was increasing in severity, had spread to involve the forehead and neck, next day he noticed painful ulcers over his palate and buccal mucosa. Patient consulted a local doctor who referred the patient to our hospital. Patient presented to Toxicology

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Address for correspondence:

Rakesh Pinninti, 12/87, 4A, B Block, Doshi Apartments, West Mada Church Street, Royapuram, Chennai, Tamil Nadu, India.

E-mail: pinninti.rakesh@gmail.com

department around 24 hrs after taking the first tablet. Patient was conscious, unable to verbally communicate due to painful ulcers in the oral mucosa and throat. Physical examination revealed patient was febrile (100°F) and tachypneic (24 cycles/minute). Patient was having confluent erythema and multiple vesicles involving most of his face with few disrupted vesicles with crusting and bleeding particularly severe around the lips, nose and forehead [Figure 1]. There were similar vesicles and few pustules over his arms, chest and abdomen [Figure 2]. We noted shallow ulcers over his palate and oral mucosa. Patient had bilateral expiratory wheeze. The extent of epidermal detachment was calculated based on Lund and Browder chart [Figure 3] and expressed as the percentage of body surface area that is involved (as for burns). Patient was diagnosed with SJS/TEN overlap syndrome and was treated with intravenous corticosteroids (methylprednisolone 125 mg), antihistamines (chlorpheniramine maleate 4 mg), fluid resuscitation with normal saline and supportive medication (iv ranitidine 50 mg). Patient developed sudden cardiac arrest around 4-5 hrs after presentation and was declared died after failed resuscitation. The temporal relation between self medication and occurrence of ADR suggests that SJS/TEN may be attributable to aceclofenac. The Naranjo adverse drug reaction probability scale score of six indicated a 'probable' relationship between SJS/TEN and aceclofenac therapy in this patient. WHO Uppsala Monitoring Centre Causality Assessment Criteria also indicated a 'probable' association with Aceclofenac.

DISCUSSION

The Stevens–Johnson syndrome and toxic epidermal necrolysis are thought to represent a single disease with a spectrum of severity.

SJS and TEN are distinguished chiefly by severity and percentage of body surface involved.^[1]

- Stevens-Johnson syndrome - SJS is the less severe condition, in which skin sloughing is limited to less than 10% of the body surface. Mucous membranes are affected in over 90% of patients, usually at two or more distinct sites (ocular, oral, and genital).
- Toxic epidermal necrolysis (TEN) involves sloughing of greater than 30% of the body surface area. Mucous membranes are involved in nearly all cases.
- SJS/TEN overlap syndrome - SJS/TEN overlap syndrome describes patients with involvement of greater than 10%, but less than 30% of body surface area.

SJS and TEN can occur in patients of any age. The mean age was higher for TEN (63 years) than for SJS (25 years). Women are comparatively at greater risk for TEN than men (ratio



Figure 1: Extensive erythematous, vesicular and pustular skin lesions associated with bleeding and adherent crusts noted over face particularly over the forehead, nose and peri-oral regions



Figure 2: Disrupted vesicles causing bleeding and crusting

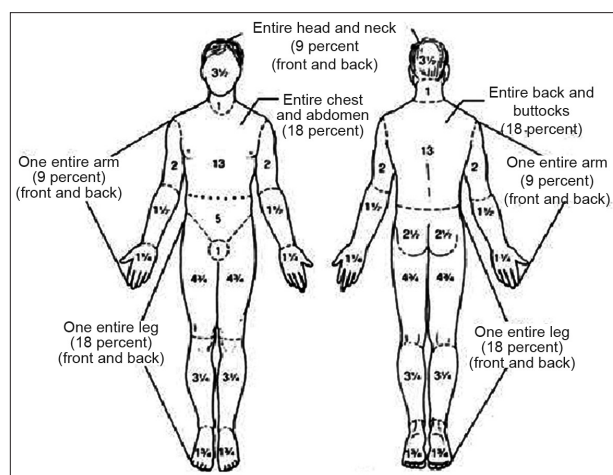


Figure 3: Lund and Browder chart

of 2:1), these figures being reversed for SJS.^[2] Medications are the leading trigger of SJS and TEN in both adults and children. In adults, medications cause 30 to 50% of cases of SJS and up to 80% of cases of TEN. The drugs most commonly involved are antibiotics (TEN, 40%; SJS, 34%), followed by the analgesics (TEN, 23%; SJS, 33%).^[2]

In one study involving 373 cases of TEN or SJS and 1720 controls, the oxicam NSAIDs (piroxicam and tenoxicam) had the highest risk (relative risk of 34) while the relative risk with diclofenac and ibuprofen were less (4.1, and 5.3, respectively).^[3]

Lapeyre-Mestre M *et al.*, analyzed data from 2002 to 2006 for aceclofenac, diclofenac, ketoprofen, meloxicam, naproxen, nimesulide, piroxicam and tenoxicam, focusing on the reported rates of serious adverse drug reactions in several organ system classes. The most frequently reported serious ADRs were cutaneous, followed by gastrointestinal, hepatic, renal and rarely cardiovascular events. Nimesulide and aceclofenac were associated with the highest risk of liver ADRs (adjusted ORs of 4.53 and 3.67, respectively).^[4]

A large multinational retrospective study of 379 patients with SJS or TEN demonstrated a non-significant trend towards diminished mortality with the administration of glucocorticoids.^[5]

Age at diagnosis and extent of skin detachment are the main prognostic factors for both SJS and TEN. Early identification and withdrawal of the offending agent improves prognosis.^[6] Any agents that could possibly be causative should be immediately discontinued in the setting of an adverse drug reaction with signs or symptoms suggestive of SJS or TEN.

Age, extent of necrolysis, idiopathic nature of toxic epidermal necrolysis, ingestion of many drugs, elevation of urea, creatinine, and glucose levels, neutropenia, lymphopenia and thrombocytopenia were statistically linked to a bad prognosis. A multivariate analysis showed that three of these prognosis factors are of paramount importance, namely: Age, area of necrolysis, and serum urea level.^[7]

The overall mortality rate for SJS has been reported to be as low as 1 to 3%.^[8] For TEN, prognosis is more guarded. More recent studies cite overall mortality rates of 25 to 35 percent.

Management involves multispecialty supportive care, which includes wound care, fluid and electrolyte management,

nutritional support, ocular care, temperature management, pain control, and monitoring for/treatment of super-infections.

Aceclofenac induced SJS/TEN overlap is an extremely rare clinical association previously reported only once in medical literature.^[9] To the best of our knowledge, this is the first case report of such an association in the Indian population.

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