ABSTRACT

Stevens Johnson’s syndrome is an exfoliative dermatitis with severe erosions of at least two mucosal surfaces including extensive necrosis of oral and nasal mucosa and purulent conjunctivitis, but less commonly involving vaginal, urethral, gastro intestinal or respiratory mucosal membranes. The Stevens-Johnson syndrome (SJS) is a rare immune-complex-mediated hypersensitivity disorder which affects 7 cases per million persons per year. This article describes a case study of a 12 year old female patient who was admitted to the tertiary care hospital, Chennai (India) with chief complaints of fever, malaise, sore throat, flu like symptoms and heavy body pain since 4 days. Burning sensation, edema, erythema of lips & buccal mucosa followed by development of bullae, ulcerations, hemorrhagic gusting since 2 days. Past history of medication revealed early clinical course of Carbamazepine for seizure prior to admission to the hospital. Based on signs and symptoms, with causality assessment analysis diagnosis of drug induced Stevens Johnson syndrome was confirmed. In the scarcity of evidence of effective treatment, patient was managed with symptomatic therapy and supportive care. As Stevens- Johnson syndrome is a potentially fatal multiorgan disease with a strong etiologic link to some medications, one must have a high index of suspicion to be able to diagnose and treat patients with SJS in time and must therefore consider Stevens-Johnson syndrome as a potential complication of treatment.

Key Words: Carbamazepine, Anti-seizure, Stevens Johnson Syndrome, Erythema and hemorrhagic gusting.
INTRODUCTION
Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare but severe cutaneous drug reactions endangering patient's life. Incidence of SJS and TEN is 2.6-7.1 persons per million populations per year in United States\(^\text{[1-2]}\). It is 1.1 and 0.93 per million per year for SJS and TEN respectively in Germany\(^\text{[3]}\). Drugs are most commonly implicated for causing 77-95% of cases\(^\text{[4-5]}\). SJS presents in three different forms which reflect the same condition: a mild form, called erythema multiforme (EM) (where <10% Total Body Surface Area is affected), the main form (between 10 and 30%), and the severe form called toxic epidermal necrolysis (TEN). Stevens-Johnson syndrome (SJS) is a serious systemic disorder with the potential for severe morbidity and even death. SJS has the mortality rate is approximately 1-5%. However, when more than 30% Body Surface Area sloughing is present, the mortality rate is between 25% and 35% \(^\text{[6-7]}\). The major causative drugs are antimicrobials, anti-epileptics and NSAIDs. Thirty three antimicrobials from 11 groups are implicated. Most common are fluoroquinolones, sulpha drugs, anti-tubercular drugs, penicillins, anti-retro virals and cephalosporins. Among the NSAIDs, paracetamol and nimesulide are most common reported in this study. SCAR study has found an overall risk of SJS with oxicam derivatives. It reports increased risk with paracetamol from Germany, Italy and Portugal except France. There is no increased risk with diclofenac, salicylates and pyrazolone derivatives\(^\text{[8]}\). Corticosteroids are considered controversial in the management of SJS/TEN despite their use for more than 30 years. No randomized controlled trials are available to establish their efficacy\(^\text{[9]}\). It is difficult to analyze the effect of steroids from this study due to limited description of their use. Early use of short term dexamethasone therapy seems beneficial. Short term dexamethasone therapy (1.5 mg/kg/day) on three consecutive days at an early stage of the reaction may reduce mortality without affecting the healing time \(^\text{[10]}\). A recent systematic review in children has shown the beneficial effect of steroids. Patients treated with dressing and support treatments alone without a steroid have longer hospitalization, remission and are more prone to complications and death\(^\text{[11]}\). HIV is the most common co-morbid condition in the patients of SJS/TEN in India. We report a case of Carbamazepine induced Stevens Johnson syndrome.

CASE STUDY
A 12 yr old female patient was from rural area of Kanchipuram (India) was admitted in pediatric intensive care unit (PICU) in tertiary care hospital, with the chief complaints of fever, malaise, sore throat, flu like symptoms and heavy body pain since 4 days. Burning
sensation, edema, erythema of lips and buccal mucosa followed by development of bullae, ulcerations and hemorrhagic gusting since 2 days (see pic-1). She had past medication history of early clinical course of Carbamazepine for seizure.

On physical examination, it was observed that patients prodrome of cutaneous lesions consists initially of erythmateous macules that rapidly & variably develop central necrosis to form vesicles, bullae, areas of denudation on face, trunk and extremities and also the involvement of 2 or more mucous surfaces namely eyes, oral cavity, upper airways, GIT, ano-genital mucosa are observed. Disseminated bullae & erosions may result in bacterial sepsis.

Laboratory investigations revealed that patient elevated level of increased erythrocyte sedimentation rate (ESR) showed inflammatory condition (The most common cause of high ESR is an increased protein level in the blood, such as the increase in acute phase protein in inflammatory disease\(^\text{(12)}\)), followed by decreased level of serum albumin showed oedema in the body (Albumin has an important role in binding, among others, calcium, bilirubin and many drugs. A reduction in serum albumin will increase free level of agents which are normally bound and adverse effect can result if the “free” entity is not rapidly cleared from the body will cause oedema\(^\text{(12)}\). Increased liver enzymes showed hepatic impairment and further with ultrasonography was confirmed. Leukocyte count also increased, it shows that sign of inflammatory response. Renal function test was normal. Other test for diabetes, malaria, HIV infections and hepatitis infections were normal.

During the hospital administration, patient was managed symptomatically for pain control, fever, burning sensation, skin and mouth ulceration. Immediately the Carbamazepine drug has been withdrowed. For supportive care the patient protected from secondary bacterial infection, maintained proper nutrition, fluid and electrolytes balance and glycerin swabs used to protect oral cavity. Proper skin dressing for fast wound healing. For systematic treatment, tobramycin eye drops with lubricant were administered. I.V. Immunoglobulin’s (1.5-2.0g/kg/day× 3 Days), short term course of parenteral corticosteroid shows the erythema reappeared from the skin (see pic-2). The dose of corticosteroid reduced gradually based on the serial laboratory reports and patient recovery. Vitamin B complex given for manages the mouth ulcers. Ceftriazone was given to cover the secondary infections. Patient recommended to physiotherapy to prevent muscle contractures. Finally the patient recovered fully and discharged on the 24\(^{th}\) day of admission with special warnings to hypersensitive drugs and
also advised some discharged medications such as, vitamin B Complex, Ceftriazone and glycerin swabs.

12 yr old female was admitted in PICU in tertiary care hospital, treatment during early clinical course of SJS due to Carbamazepine

Same patient during the late clinical course of SJS

CONCLUSION

Stevens Johnson syndrome is potentially fatal condition of skin & mucus membrane but can also affect other vital organs. Patients safety is prime important while physician treating the patient and lack of physician knowledge in drugs, improper guidance by the pharmacist, lack of patient counseling, poor patient memories are the factor to exist such kind of syndromes in human beings. Clinical pharmacist knowledge is equal important to the management of all disease and disorders. Now a day’s ‘N’ number of drugs reported that causing ADR’s and side effect in Indian population, so proper guidance and advice (from physician and clinical pharmacist) is necessary to avoid the existence of such kind of ADR’s and side effects. Commonly some of the drugs like Carbamazepine, Phenobarbital, Phenytoin and Valproic acid have high incidence to cause SJS/TEN and also these minds of reactions are independent on dose of drug and are idiosyncratic \[^{13}\]. A study with adverse reactions of SJS/TEN due to anti-seizure drugs revealed that they had the higher chance (81.8%) of causing severe eruption, that is SJS/TEN than NSAIDs (53.84%) and antimicrobials (34.48%). This is higher as compared with the previous report (70%) \[^{14}\]. The exact mechanism of SJS/TEN still remains largely unknown. In immunological mechanisms reactive drug metabolites or
interactions between these two are proposed. Interactions between CD95 L and Fas (CD 95) are directly involved in the epidermal necrolysis. Granulysin is also considered as a key mediator for disseminated keratinocyte death in SJS/TEN \[15\]. Evidence has shown various pathological mechanism like drug specific CD8+ cytotoxic lymphocytes, natural killer cell activation, cytokines including perforin/granzyme, Fas-L and Tumour Necrosis Factor (TNF) alpha \[16\]. Cytokines play a role in the immune-pathological and molecular mechanisms of drug-induced hypersensitivity reactions (HSR). A study of Carbamazepine induced Stevens Johnson Syndrome in the patient with high level of TNF-alpha, leucocys, ESR and decreased level of serum albumin showed inflammatory response in the body through hypersensitivity reaction. Finally this case study were expressed the use of immunoglobulin’s and corticosteroids for the treatment of Stevens Johnson Syndrome with potential complications. Patient has to cooperate well to the physician and proper review also a peak important for the fast recovery of patients from SJS/TEN.

REFERENCE


