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Ceftriaxone induced Stevens-Johnson syndrome and toxic epidermal necrolysis (SJS/TEN) overlap in an elderly patient: A Rare Case Report

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Abstract

Stevens Johnson Syndrome (SJS)- Toxic Epidermal Necrolysis (TEN) overlap are rare epidermolytic adverse cutaneous drug reactions with incidence of 1-10 cases per 1 million per year. It is a severe delayed hypersensitivity reaction following drug exposure and may lead to significant morbidity and mortality in the genetically predisposed. This article describes a rare case report of a 74 year-old -elderly female, who presented to Pravara Rural Hospital, Ahmednagar, Maharashtra with blisters, peeling of skin on neck, mouth, groin, chest with difficulty in swallowing since 30 days. Patient complained of skin ulcers after ingestion of ceftriaxone prescribed by a local doctor which was ignored by her. Gradually the lesions became erythematous, scaly, tender and were associated with widespread mucocutaneous blistering and exudates. Based on signs and symptoms of the patient, she was diagnosed as a case of Stevens Johnson Syndrome/ Toxic Epidermal Necrolysis (SJS/TEN) Overlap. She was immediately admitted and managed conservatively with antibiotics, steroids, cyclosporine, supportive measures like correction of electrolyte imbalance and topical symptomatic treatment for skin lesions. This case is being reported to emphasize the fact that, pharmacovigilance ensures drugs are safe and improve patient care and this is possible by reporting of adverse drug reactions.

Keywords: Stevens Johnson Syndrome, Toxic Epidermal Necrolysis, Adverse drug reaction, ceftriaxone.

Introduction

Cutaneous drug reactions are one of the most frequent manifestation of adverse drug reactions.1 Adverse cutaneous reactions to drugs are found to affect 2-3% of

all hospitalized patients.2 Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and Stevens-Johnson/toxic epidermal necrolysis overlap syndrome are rare but severe delayed-type drug hypersensitivity reaction and constitute medical emergency as they are associated with high morbidity and mortality.3 They presents with widespread blistering, ulceration and necrosis of the skin and mucosa in the genetically predisposed.

The distinguishing factor between SJS and TEN is the degree of body surface area involvement. SJS is considered a minor form of TEN which is characterized by less than 10% involvement in total body surface area, 10%-30% involvement in SJS/TEN overlap whereas >30% in TEN.4 (Fig 1)

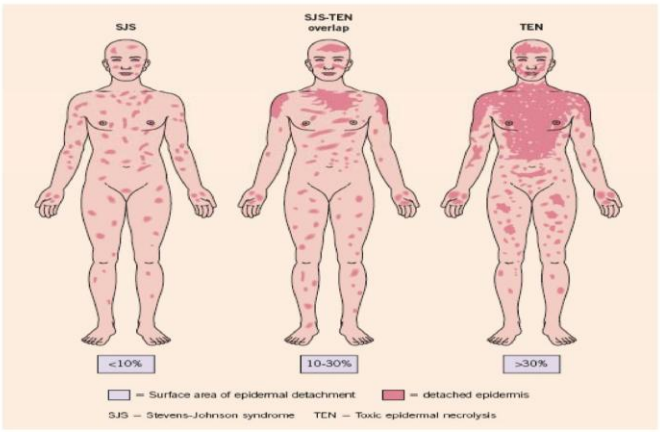

Fig. 1: Pictural representation of SJS, SJS-TEN overlap and TEN showing the surface of epidermal detachment (Adapted from Fig 21.9 Bolognia and Bastuji-Garin S. et al. Arch Derm 129: 92, 1993.

The pathogenesis of SJS/TEN is not fully understood but is believed to be immunemediated. keratinocyte apoptosis followed by necrosis is the pathogenic basis of the widespread epidermal detachment observed in SJS/TEN. The clinical, histopathological and immunological findings in SJS/TEN show that SJS and TEN are specific drug hypersensitivity reactions in which cytotoxic T lymphocytes (CTL) play a role in the initiation phase.5,6. Studies have shown that CD8 T-cells as well as the cytolytic molecules FasL and granulysin are key players in the pathogenesis of SJS/ TEN7. It is the subject of ongoing research on how a culprit drug in a given patient who will develop SJS/TEN regulates the function of these key players.

Case Report

A 74 years old female patient from rural area of Ahmednagar district in Maharashtra presented to the emergency department of Pravara Rural Hospital with epigastric pain and blisters, peeling of the skin and burning sensation on lips, face, neck, mouth , groin, chest region with difficulty in swallowing since 30 days. One month before her presentation, patient had history of taking ceftriaxone prescribed by a local doctor, after which she started developing skin lesions, which were ignored by the patient.

The patient had also complained of epigastric pain since one month, for which she consulted a local doctor. Upper GI endoscopy was done15 day's back which revealed esophagitis with small ulcer at the oropharynx. This was also ignored by the patient. The skin lesions gradually became scaly, tender and there was extensive mucocutaneous blistering with exudative ulcers over the back and flexors after which she presented to our emergency department and was immediately admitted for management. There was around 20% body surface area involvement of the skin lesions in the patient.

Fig.2: Extensive mucocutanous blistering on lips, face, mouth

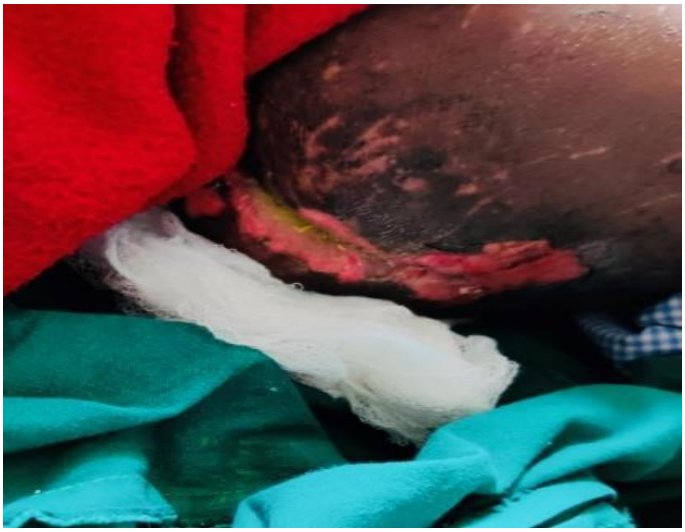

Fig.3: Exudating ulcer over the back

Fig.4: Multiple Scaly lesions with ulceration base on back

The patients initial vital signs were blood pressure, 136/110 mm Hg ; Pulse-100 beats per minute ; respiratory rate 22; and temperature, 101.9. Complete blood count, serum electrolytes, renal function tests, liver function tests, coagulation profile were unremarkable. The Naranjo Adverse Drug Reaction Probability Scale score of 6 was derived suggesting **Probable** association between ceftriaxone and the adverse drug hypersensitivity reaction. The patient was not taking any other medication prior to ingestion of ceftriaxone. A diagnosis of Stevens Johnson Syndrome/Toxic Epidermal Necrolysis overlap was made.

The patient was managed rigorously at Pravara Rural Hospital and a multidisciplinary team was involved in her care, including medicine, dermatology, surgery and Oral medicine departments. During the hospital stay, patient was managed symptomatically for pain control, skin and mouth blistering and ulceration. The patient improved after initiation of intravenous methylprednisolone along with fluid replacement as supportive therapy. Corticosteriod dose was gradually tapered from sixth day of the treatment. Cyclosprine was also given to the patient twice daily. For congestion in eyes and eye lesions, moxifloxacin eye drops with lubricant drops were given thrice daily. Broad spectrum antibiotics were given to cover the gram positive and gram negative infections. Topical Mupirocin ointment was given to apply on the skin lesions thrice daily. High Protein diet and plain water compresses on the lesions were adviced to the patient. Xylocaine for symptomatic improvement in mouth ulcer along with mutlivitamins to aid wound healing were given.

Patient recovered gradually after one month of rigorous treatment and was discharged on 30th day with a warning card for sensitivity to drug to avoid any such incidence in the future. On discharge, patient was adviced to continue

cyclosporine for 7 days, multivitamins were given with lubricant eye drops and was told for follow up after 7 days.

Discussion

SJS/TEN aetiologies include reaction to drugs like Penicillin, Sulphonamide, Phenytoin, Valproate, Carbamazepine, non-steroidal anti-inflammatory drugs, antimalarial and allopurinol8,9. Coxsackievirus, Echovirus, Herpes Simplex viruses and Mycoplasma infections have also been linked to this syndrome in some cases.

Similarly SJS has also been associated with immunisation, e.g. measles and hepatitis B10. However, in approximately 25 to 50 percent of cases no cause can be identified. In our case, patient had cutaneous manifestation after administration of ceftriaxone.

There is evidence regarding the association of cephalosporin as the culprit for SJS/TEN. This group of drug is considered the 5th most common among antibiotics giving rise to SJS/TEN11. SJS is a fatal condition, with a global mortality rate stretching between 10% and 34%, thus warrants early identification and treatment based on a multidisciplinary approach[12].

There is no standard procedure to validate the etiology of the causative drug in SJS/TEN cases. Positive history of intake of inflicting agent is the most strong evidence as not having any confirmatory research tools sufficient to identify the causative agent. Hence, identification of the first incident of adverse drug reaction is based on the probability estimation and evaluation13. The management is mainly focussed on supportive care , correction of fluid and electrolyte imbalance, pain relief, prevention of infection, prevention and treatment with sterile handling of skin, oral and eye lesions. Medical therapies, including systemic glucocorticoids, cyclosporine, tacrolimus, and IV immunoglobulin, have been used in small cohorts, but their role is variable and unclear14. The case under consideration received corticosteroids with cyclosporine in addition to supportive measures.

Adverse drug reactions which are said to be a cause of morbidity, disability, mortality as well as economic drain in the health system, accounts for about 4.9% of hospital admissions worldwide15. However, it is under-reported mostly in developing countries and even in developed countries16. Therefore, understanding and reporting adverse drug reaction is very important in everyday clinical practice.

Conclusion

Ceftraixone is the most commonly prescribed cephlosporin by most of the physicians in a developing country like India owing to its high efficacy and cost effectiveness. Judicious and cautious use of antibiotics is the need of the hour. Mindful presciribing by the physicians and reporting of slightest cutaneous manifestations by patients plays a huge role in preventing the consequences in such cases. SJS, TEN and SJS/TEN overlap can be fatal,life threatening condition, if not treated timely.

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