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A CASE REPORT OF STEVEN JOHNSON SYNDROME AND TOXIC EPIDERMAL NECROLYSIS OVERLAP SYNDROME DUE TO COTRIMOXAZOLE IN HIV INFECTED PATIENT AS ADVERSE DRUG REACTION

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ABSTRACT Cotrimoxazole is an antibiotic used to treat certain bacterial infections like pneumonia and bronchitis. It is a combination of Sulfamethoxazole and Trimethoprim. It is commonly used for the management of several uncomplicated infections, treatment and prophylaxis of Pneumocystis jiroveci pneumonia (PCP) in the HIV infected population. It is known to produce several serious ADRs like SJS and TEN. This is a case report regarding 43years old woman presented with an erythematous rash with desquamation was admitted in Dermatology ward Government General Hospital, Vijayawada. Multiple erythematous red dusky macules involving face, neck, trunk, abdomen and extremities and Oral lesions with erythematous base present over lips and oral mucosa. She was being treated with Highly Active Antiretroviral Therapy from the past 6 months which included Efavirenz, Lamivudine, and Tenofovir. One week back she was treated with Cotrimoxazole tablets prescribed by a local physician for the complaint of fever. She developed SJS and TEN overlap syndrome after 4 days. Dechallenge was done. She was treated with intravenous fluids and Inj.Decadron. She improved gradually in six days. **Results:** The Erythematous rash with desquamation of skin due to Cotrimoxazole was considered as a probable adverse reaction after Dechallenge to the drug (As per WHO scale). The reaction subsided gradually. Rechallenge was not done. ADR reported was reported to ADR monitoring center and uploaded in Vigiflow. **Conclusions:** As the patient showed a positive response after dechallenge, this implies the contribution of Cotrimoxazole to the skin reaction. Due to the high incidence of such hypersensitivity reactions, physicians should monitor HIV-infected patients on Trimethoprim-Sulfamethoxazole therapy.

KEYWORDS : Steven Johnson syndrome, Toxic epidermal necrosis, Cotrimoxazole, sulfamethoxazole-trimethoprim

INTRODUCTION

Toxic epidermal necrolysis (TEN) and Stevens-Johnson Syndrome (SJS) are severe cutaneous adverse drug reactions.(1) They are rare, life-threatening conditions usually involve the skin and mucous membranes. They are severe forms of exfoliative dermatitis and characterized by extensive epidermal erythema and blistering, which leads to necrosis and detachment of the epidermis and can also cause mucocutaneous lesions.[2]

SJS, first described in 1922, comprises extensive EM of the trunk and mucous membranes accompanied by fever, myalgia, malaise, and arthralgia. TEN was first reported in 1956 by Lyell, which was characterized by extensive, skin erosions with widespread purpuric macules or lesions which are flat, atypical accompanied by severe involvement of the conjunctival, corneal, buccal, labial and genital mucous membranes.[3]

To distinguish SJS, SJS-TEN and TEN the surface area of the detachment is the main discriminating factor.(1) This case reporting was done to sensitize the prescribers regarding rare side effects of the above drug.

CASE REPORT

History :

43years old woman presented with an erythematous rash with desquamation was admitted in Dermatology ward Government General Hospital, Kakinada. Multiple erythematous red dusky macules involving face, neck, trunk, abdomen and extremities and Oral lesions with erythematous base present over lips and oral mucosa. She was being treated with Highly Active Antiretroviral Therapy from the past 6 months which included Efavirenz, Lamivudine, and Tenofovir.

The past medical history revealed that the patient was suffering from fever and pain for 7 days. She was prescribed tablet Cotrimoxazole for fever and pain by a local medical practitioner. The patient was relieved from fever and pain but later she had a burning sensation followed by ulcers in the oral cavity and extra-oral surface. The patient visited the hospital after 4 days of lesion appearance(Figure 1, 2 & 3). Considering the history, clinical examination, and laboratory findings, the patient was diagnosed as a case of Cotrimoxazole induced SJS and TEN overlap syndrome. Dechallenge was done. The patient was treated under the expert guidance of dermatologist with intravenous fluids and Inj.Decadron. She improved gradually in six days. The Naranjo probability score was 7, suggesting probable drug reaction.

Figure 1: Patient with oral involvement SJS-TEN overlap, 5 days after the use of cotrimoxazole.

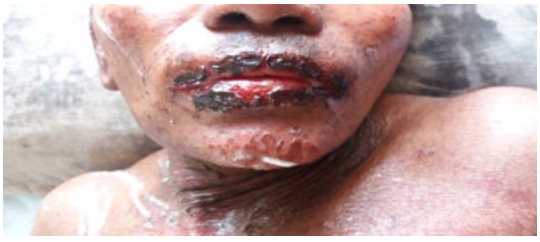
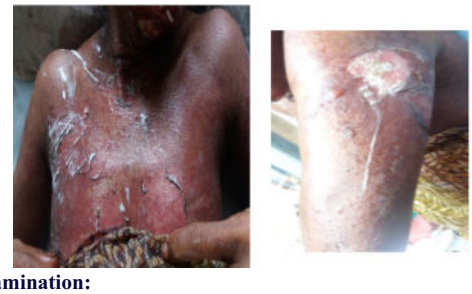


Figure 2 & 3: Patient with SJS-TEN overlap, 5 days after the use of cotrimoxazole



On examination:

We made a diagnosis of SJS-TEN overlap syndrome in our case based on the history of drug exposure with a typical clinical manifestation of erythema, blistering and detachment of skin involving >25% of BSA, and it is supported by typical histological findings and laboratory investigations which revealed leukocytosis, Hemoglobin - 7.8 gm %, Total leucocyte count- 9,500 cells/mm^3, CD4 count - 197 cells, Serum Bilirubin- 0.3 mg/dl, SGOT- 12 IU/L, SGPT- 24 IU/L, ALP- 96 IU/L, Blood urea-37 mg/dl.

There was no history of any drug allergy and the rest of her medications were not reported to cause SJS or TEN. Furthermore, she had used her regular medications for many years without severe skin disease.

DISCUSSION

Cutaneous adverse drug reactions (CADRs) are very common in the dermatology outpatient department. SJS or TEN is one of the dermatologic conditions that can be fatal. SJS is the less extensive form and TEN is the more extensive form. The extent of total skin surface involvement is less than 10% in SJS, and it is more than 30% skin involvement in TEN, while 10%–30% is designated as SJS/TEN overlap syndrome.[4]

Toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS) are acute life-threatening mucocutaneous reactions. The epidemiology and causative drugs differ significantly in different ethnic populations due to genetic factors.[2] Usually, it is believed to be an immune-mediated hypersensitivity reaction in which cytotoxic T lymphocytes play an important role in the pathogenesis.[4] In clinical practice, these reactions are usually due to drug-induced hypersensitivity. The etiological factors vary from viral infections to various pharmacological agents.[5]

The drugs that cause Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) are Allopurinol, Carbamazepine, Lamotrigine, Nevirapine, non-steroidal anti-inflammatory drugs, Phenobarbital, Phenytoin, Sulfamethoxazole, and others.[6]

The diagnosis is based on both clinical symptoms and on histological features. The extent of skin involvement is a major prognostic factor.[1] As the course of the disease is often rapid and fatal, Early diagnosis of the disease, and recognition of the agent responsible and the immediate withdrawal of the drug that is responsible are most important.[4]

The increased incidence of adverse reactions to TMP/SMX in HIV-infected patients is due to sulphamethaxazole hydroxylamine which is the hydroxylamine derivative of sulphamethaxazole. In HIV-infected patients the deficiency of glutathione enzyme results in a decreased capacity to scavenge these hydroxylamine derivatives.[7]

Veenstra *et al*. found that patients with adverse reactions to TMP/SMX have a more rapid decline in CD4 cell counts and rapid progression to AIDS and death.[8] So as soon as the diagnosis of SJS or TEN has been established, we have to assess the severity and prognosis of the disease so we can decide the appropriate medical setting for further management of the patient.

In the acute stage of disease, the management first involves evaluation of the severity and prognosis of disease, identification, and withdrawal of the culprit drug, and initiating supportive care, and specific drug therapy has to be given.[1] Garcia-Doval *et al*., reported that earlier the drug is withdrawn, better the prognosis, while exposure to drugs with longer half-lives increases the risk of death.[9]

In order to evaluate the prognosis in patients with SJS/TEN, the validated SCORTEN which is a disease severity scoring system can be used. The SCORTEN severity-of-illness score is now the most widely used scoring system and it evaluates the following parameters: Age > 40 years, malignancy, tachycardia, Initial surface of epidermal detachment >10%, Serum urea >10 mmol/l, Serum glucose >14 mmol/l, Bicarbonate >20 mmol/l. If the features are present then score is 1 for each yes and 0 if it is NO. Patients with a SCORTEN score of 3 or above if possible they should be managed in an intensive care unit.[10] Supportive measures include control of body temperature, hydration, and electrolyte replacement, special attention to the airways, pain control, preventing secondary infection, early oral nutrition.[4] Debridement of necrotic skin should not be performed before disease activity ceases.[11]

The differential diagnoses include disorders involving the peeling of the skin, such as erythema multiforme major, burns, widespread fixed drug eruption, herpes simplex virus (HSV)–associated erythema multiforme, erythroderma, bullous pemphigoid, acute generalized exanthematous pustulosis, linear IgA dermatosis, paraneoplastic pemphigus, lymphoma, viral rashes, staphylococcal scalded skin syndrome, secondary syphilis, herpetic gingivostomatitis, graft versus host disease and autoimmune vasculitis.[12]

Alternative systemic treatment methods for SJS-TEN include intravenous immunoglobulin, hemodialysis, plasmapheresis, cyclosporine, and cyclophosphamide.[13]

CONCLUSION

The Erythematous rash with desquamation of skin was considered as a probable adverse reaction due to cotrimoxazole. And as the patient showed a positive response after dechallenge, this implies the contribution of Cotrimoxazole to the skin reaction. It is believed to be immune-mediated. Re-challenging is not done in this case because the same drug can result in rapid recurrence of SJS/TEN.

This reaction was reported to ADR monitoring center and uploaded through Vigiflow

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Ethical approval: The study was approved by the Institutional Ethics committee of Siddhartha medical college, Vijayawada, India

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