Cefixime Induced Stevens-Johnson Syndrome: A case report and Review of literature

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ABSTRACT

Introduction: Stevens–Johnson syndrome (SJS) is one of the manifestations of severe form of cutaneous adverse drug reactions (CADRs). It is an acute, self-limited disease, presenting as severe mucosal erosions with widespread erythematous, cutaneous macules or atypical targets. Majority of the SJS cases are drug-induced despite its varied etiology.
Case report: We report here a case of 55 years old woman who reported us with the chief complaints of rash with erythema of conjunctiva and crusting of the eyelids, fever, and dysphagia. The rashes appeared after four days of consumption of tablet cefixime hydrochloride (200 mg) twice daily for LRTI with fever. She was treated conservatively and tablet cefixime was stopped, oral and eye lesions were taken care of. Causality assessment using the WHO UMC criteria and Naranjo's algorithm revealed that the adverse drug reaction (ADR) was 'probable'. With ALDENS algorithm, the causality was 'very probable', and Preventibility score as determined using Schumocks and Thorntons criteria revealed the ADR to be 'preventable'.
Conclusion: Although there are ample cases of SJS due to beta-lactam antibiotics in the literature, few reports of cefixime-induced SJS are in record till date. Hence, motivation of the healthcare professionals is of utmost importance in order to avoid such adverse drug reactions, which in turn may result in strengthening of the pharmacovigilance program in India as well as enrichment of rational drug prescribing.

Keywords: Cefixime, CADR, Stevens-Johnson syndrome, rational drug therapy

INTRODUCTION

Modern day drug therapy has made great strides in the recent past and adverse drug reaction(ADR) remains to be major threat in the management of patients. Stevens-Johnson Syndrome (SJS) is one such serious ADR, which was described as a severe variant of erythema multiforme as "A new eruptive fever with stomatitis and opthalmia" and termed as SJS by Albert Mason Stevens and Frank Chambliss Johnson in 1922.[1] SJS is a severe hypersensitivity reaction that can be precipitated by infection such as herpes simplex virus or mycoplasma, vaccination, systemic diseases, physical agents, food and drugs.[2,3] Such severe idiosyncratic adverse drug reactions are characterized by a low incidence but high mortality. SJS is generally diagnosed by a dermatologist using Bastuji Garin classification.[4] The incidence of SJS is approximately six cases per million persons per year, and that of TEN is approximately two cases per million persons per year.[5] Previously mortality could be decreased by improving the supportive care only due to lack of specific therapy. But, recently intravenous immunoglobulin (IVIG) has emerged as a promising therapeutic option.[6] The drugs that cause SJS commonly are antimicrobials, anticonvulsants, NSAIDs, and oxide inhibitors.[7] Among the antimicrobials as causative agent of SJS, antiretrovirals are the most common group, followed by the anti-tubercular drugs, sulphonamides, fluroquinolones, and penicillins.[5]

CASE REPORT

A woman aged 55 years attended the medicine outpatient door (OPD) of a tertiary care hospital with the chief complaints of rash over face, neck, upper part of chest and both the hands for three days. She also complained of dysphagia, fever, and erosive stomatitis with drooling. On examination, the rashes were tender,pruritic, maculopapular and erythemetous in nature with multiple excoriations of both the upper and lower lips and upper lids of the eyes. Opthalmological examination revealed bilateral upper lid crusting and excoriation, conjuctival congestion and superficial keratitis. She had normal visual acuity, and findings of direct opthalmoscopy and slit-lamp examination were within normal limits. General examination revealed pulse=86/minute, BP= 130/80 mm of Hg, raised body temperature (102 degree farenheit) with absence of oedema, pallor, jaundice, cyanosis and clubbing. No visceral tenderness or organomegaly was found on systemic examination. Laboratory investigations incuding complete haemogram, liver function test, and renal function test was normal. History taking revealed, oral intake of tablet cefixime hydrochloride (200mg) twice daily for four days for lower respiratory tract infection (LRTI) with fever after which the rashes started appearing on the fifth day, firstly over the forehead followed by progression over the entire face, lips and both the eyes. The rashes then gradually spread to the neck, upper part of chest and both the hands with lesser involvement of the back of chest, abdomen and lower limbs. She also had ulcers over the oral mucosa. The patient came to the OPD on seventh day of the suspected drug intake. She had no previous history of any drug hypersensitivity reactions. She was being co-prescribed tablet paracetamol (650 mg) every 6 hours for the control of fever and an expectorant syrup 10 ml (2 teaspoons) 3 times a day for her cough symptoms along with the tablet cefixime hydrochloride. She was then admitted to the hospital, Tablet cefixime was stopped and the patient was treated conservatively without discontinuation of the other two medications. Her eye lesions were treated with eyedrops moxifloxacin, homatropine, carboxymethylcellulose, and tobramycin ointment. Further progression of the rashes was halted and the patient started recovering within the two days of withdrawal of tablet Cefixime. Tablet Cefixime was not rechallenged or reinstituted as the patient refused to give informed consent for the sake of her own health. Causality assessment using the WHO UMC

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Figure-1: Multiple excoriations of upper and lower lips; **Figures-2 and 3:** Upper lid crusting and excoriation, conjuctival congestion and superficial keratitis in both the eyes

criteria[8] and Naranjo's algorithm[9] revealed that the adverse drug reaction (ADR) was probable. The causality was not certain as there was no rechallenge and the drug level was also unknown as required for Naranjo's algorithm. With ALDENS algorithm,[10] the causality was very probable,and Preventibility score as determined using Schumocks and Thorntons criteria[11] revealed the ADR to be preventable. The patient was then prescribed tablet levofloxacin (750 mg) once daily for 5 days, for her LRTI by the consultant physician as the rashes gradually resolved over a week.

DISCUSSION

Recent data of drug induced SJS have shown the antimicrobials to be the most commonly suspected drugs (45%) as has also been reported in Australia.[12] It is postulated that in some individuals, due to a genetic defect, the drug metabolites may bind to the proteins and trigger an immune response may bind to the proteins and trigger an immune response that leads to the cutaneous reactions of SJS.[13] Literature search could not reveal cefixime induced SJS so commonly in adults as compared to children. Our case did not reveal similar occurrence in the past with the history of intake of other medications and specifically with any other antimicrobials specially belonging to the beta lactam class or any other class. Hence, FDE can be ruled out clearly in our case. Other differential diagnosis such as DRESS, EM, TEN, exanthematous drig eruption, and lichenoid drug eruption were ruled out in this case. Causality assessment revealed that the ADR was probable according to WHO UMC scale and Naranjo's algorithm. ALDENS algorithm showed causality was very probable,and Preventibility score as determined using Schumocks and Thorntons criteria revealed the ADR to be preventable in nature. Skin detachment <10% of body surface area (BSA) with widespread erythematous or purpuric macules and involvement of the mucous membrane confirms the diagnosis of SJS in our case.

CONCLUSION

This case is probable and clinically confirmed case of SJS that is a serious and life threatening adverse drug reaction especially when caused by unknown drugs, those drugs used for self-medication as well as over the counter (OTC) drugs. This may in turn pose a greater challenge in the diagnosis and management of such cases. A dynamic and robust ADR monitoring system with a scope of feedback to and from the prescribers, and education of the prescribers may be helpful in the prevention, identification and management of drug induced SJS much more effectively.

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