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Case Study

STEVENS-JOHNSON SYNDROME DUE TO ADVERSE DRUG REACTIONS: A CASE SERIES

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ABSTRACT

Stevens-Johnson syndrome (SJS) is a rare, serious disorder affecting skin and mucous membranes. It is one of the few serious dermatological adverse effects of drugs encountered in clinical practice which is characterized by blisters and rash on skin, mucous membranes, swelling over face and lips, and hyperpigmentation. After that, the outer layer of affected skin becomes dead, sheds, and starts to heal after several days of inflicting injury. Here, we present a case series of ofloxacin and chloroquine induced SJS after the consent given by patients. First case is a 62 years old male received Ofloxacin and second patient is a 40 years old male received chloroquine. Both patients experienced a severe skin reaction which was diagnosed as SJS. The above-mentioned medications will be implicated in cases of SJS. We should prescribe these medications with extreme caution.

Keywords: Stevens-Johnson syndrome, Ofloxacin, Chloroquine, Blisters,

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INTRODUCTION

Stevens-Johnson syndrome (SJS) is a serious unfavorable mucocutaneous drug reaction mainly affecting the skin and mucous membranes. This is basically an immune-mediated hypersensitivity reaction [1] and most commonly associated with drug exposure [2]. Ofloxacin is one of the most commonly used fluoroquinolone because of easy accessibility, availability and cost-benefit ratio. Chloroquine is also a commonly prescribed drug for malaria, rheumatoid arthritis, and amoebic liver abscess. Both the drugs are considered as comparatively safer, but undesirable, untoward adverse effects mainly cutaneous hypersensitivity reactions have been reported in only few instances due to these drugs [3,4].

Consent from patients

Both the patients of this case series gave consent for manuscript preparation and submission.

CASE PRESENTATIONS

Patient 1

A 62-year-old male patient presented in dermatology outpatients department with complaints of rapidly progressive rashes which became hyperpigmented on all over his body. Patient gave a positive history of abdominal pain with associated diarrhea for which he took ofloxacin tablets. On the next day, he developed acute generalized erythematous rashes with itching all over his body including face, upper and lower extremities, scalp, and trunk. He also developed erosive lesions over oral mucosa and mild congestion in his conjunctiva (Figs. 1 and 2).

On the examination, patient was conscious, well oriented to time, place and person and stable with mild febrile condition (38.5°C) and hypotensive (102/72 mm Hg). Pulse rate was 76 bpm and respiratory rate was 21/min. Blister formation on some parts of body was also present. Erosion and crusting over lip was also noticed. There was no hepatosplenomegaly or lymphadenopathy.

Platelet count in this patient was normal and his total white blood cell (WBC) count was 4.98×109/L. His hemoglobin value was 12.3 g/dl. Liver function tests showed mild elevation in alanine aminotransferase (703 U/L) and aspartate aminotransferase (92 U/L) level. Erythrocyte sedimentation rate (ESR) was 54 mm/h. Serum creatinine was 1.2 mg/dl. Systemic examinations did not tell any significant findings. Other laboratory findings were within normal range.

On the basis of history, clinical examinations and findings, this patient was diagnosed as a case of SJS which is due to ofloxacin intake. Patient was admitted in the hospital and treated with antihistamines, intravenously (IV) administered dexamethasone (4 mg/day for 5 days) and 2% fusidic acid cream was applied topically. Carboxymethyl cellulose eye drop was also prescribed for the relief in conjunctival congestion and irritation. Later he was continued on tablet methyl prednisolone 20 mg/day. Intravenous fluid therapy, symptomatic, and supportive treatment had been done for optimum care of the patient. He showed significant improvement in his condition within 12 days. Then patient was discharged with oral steroid. Dose of steroid was tapered gradually over next 2 weeks. Almost all lesions totally resolved in a few weeks leaving post-inflammatory hyperpigmentation over his body without any other complications.

Patient 2

A 40 years old male was brought to the emergency department of the hospital with painful skin rashes, blisters, and erosions all over the body accompanied by fever and myalgia. It started on the 2nd day during the course of chloroquine therapy given by a local practitioner for empirical treatment of malaria. The rashes appeared on the trunk initially (Fig. 3) and then slowly progressed to involve the extremities and mouth also. Rashes were papular erythematous eruptions coupled with itching. The lesions became hyperpigmented later on. On the basis of history, clinical examinations and relevant findings, he was diagnosed as a case of SJS induced by chloroquine. He also had difficulty in swallowing due to painful erosions of the mouth and oropharynx. It was associated with bilateral conjunctivitis but there was no visual impairment. His hemoglobin value was 13.4 g/dl and platelets were in normal range. The total WBCs count was 8.1×10^9/L along with normal liver and renal function tests. Serum creatinine was 1.1 mg/dl. ESR was 25 mm/h. Investigations also showed the negative findings for malaria parasite and Widal test. Systemic examinations did not tell any relevant findings. Other laboratory values and findings were within the normal limits.

Patient was admitted and treated for 1 week with IV fluids, injection ceftriaxone 1 g, 12 hourly, IV after sensitivity testing to prevent secondary infections, injection hydrocortisone 100 mg, 8 hourly IV, tablet ranitidine 150 mg BD, tablet cetirizine 10 mg OD, local application of glycerine for soothing effect and fusidic acid cream (2%)

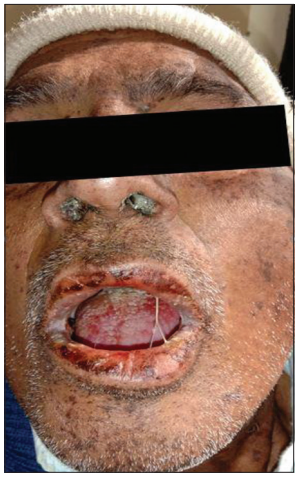

Fig. 1: Erosive lesions over oral mucosa

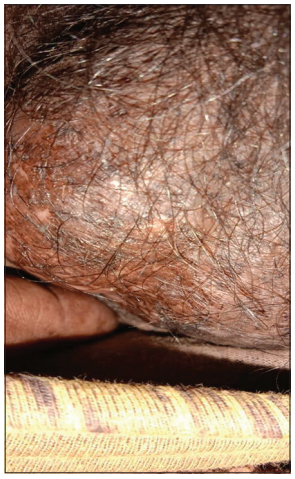

Fig. 2: Erythematous rashes over scalp

as antiseptic for 7 days. Finally, the patient improved and discharged successfully.

There was no history of any drug allergy and he had not taken chloroquine in the past. No other drugs were taken concomitantly. Other blistering skin diseases like bullous pemphigoid and pemphigus vulgaris were excluded from the diagnosis on the basis of clinical grounds.

Thus, the above-mentioned SJS has a strong temporal association to chloroquine intake. However, rechallenge is not justified in this case due to ethical constraints and fatal outcomes. This adverse reaction is not dose related. It can be considered as Probable/Likely adverse drug reaction as per causality assessment of suspected adverse drug reactions [5].

DISCUSSION

The pathogenesis of SJS is not fully understood, but is believed to be an immune-mediated hypersensitivity reaction. The clinical, histopathological, and immunological findings in SJS support the concept that SJS is a specific drug hypersensitivity adverse reaction in which cytotoxic T lymphocytes play predominant role in the initiation phase of the reaction [6]. The estimated incidence of the SJS ranges between 1.2 and 6/million populations/year but the mortality rate is nearly 15%. HIV positive patients appear to be at an enhanced risk of developing the SJS.

The use of fluoroquinolones like ofloxacin has been increasing due to their broad spectrum antimicrobial action, easy availability, and

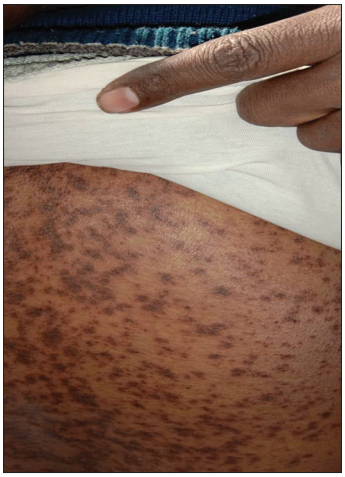

Fig. 3: Rashes over trunk

fewer side effects. Until now, these drugs have seldom been implicated in patients with SJS, but the incidence of fluoroquinolone-induced cutaneous drug reactions may be on the rise. There are very few reports of antimalarial drug chloroquine evoked SJS; however, it is usually unnoticed in its adverse result profile.

Injudicious uses of antibiotics are the foremost common reasons behind SJS, followed by analgesic drugs, cold and cough medications, antipsychotic drugs, antiepileptics, and allopurinol within the general population. Among antibiotics, penicillin, and sulpha drugs are main culprit and very few cases of chloroquine and fluoroquinolone induced SJS are also reported [7]. Some of these drugs may also be adulterated because of increased access through the internet and no strict regulation on their sale in the market.

Thus, the idea of this written statement is to create awareness about the rare but potentially fatal drug reaction such as SJS with ofloxacin and chloroquine which is commonly used for the treatment of bacterial infections and malaria, respectively, in India and in other countries.

CONCLUSION

The side effects of fluoroquinolones such as ofloxacin and chloroquine now be broadened to rarely include SJS and should be considered in patients presenting with similar clinical features and manifestations in the form of mucocutaneous side effects due to these offending drugs. As with other symptoms more commonly associated with this condition, these may resolve after discontinuation of the offending medication. Further studies are warranted to elucidate the relationship and the mechanism by which ofloxacin and chloroquine can cause SJS.

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AUTHORS CONTRIBUTION

Zafar Masood Ansari and Bhavana Srivastava contributed in writing the manuscript whereas Arunima Rohatgi and Kalpana Joshi provided the particulars and details of the patients.

CONFLICTS OF INTEREST

Nil.

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