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Topical Gatifloxacin induced Stevens Johnson Syndrome - A Case Report

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ABSTRACT

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are life-threatening severe cutaneous drug reactions. Skin and mucous membrane are mainly involved, characterized by necrosis, detachment of epidermis and exfoliation of the mucosa. The involvement of mucus membrane is further complicated by sepsis, gastrointestinal bleeding, and abnormalities of ocular and genitourinary systems, respiratory failure and death. Gatifloxacin is an antibiotic belong to the fourth-generation fluoroquinolone family. It works by inhibiting the bacterial enzymes DNA gyrase and topoisomerase IV. Systemic administration of Gatifloxacin was banned due to fluctuation in blood glucose levels. It was introduced in 1999 for the treatment of respiratory tract infections. Gatifloxacin ophthalmic solution is used to treat bacterial conjunctivitis in adults and children. We describe a case of 65 year old male with history of conjunctivitis presented in the general medicine clinic with complaints of mouth ulcers. On evaluation of the medication history it was assessed that the patient was given Gatifloxacin eye drops for the treatment of bacterial conjunctivitis. Blisters in mouth later leading to Steven Johnson Syndrome appeared after topical application of Gatifloxacin. Though Stevens Johnson Syndrome can be fatal, patient responded well to the treatment.

INTRODUCTION

Gatifloxacin is a synthetic broad-spectrum 8-methoxyfluoroquinolone antibacterial agent. It is bactericidal and its mode of action depends on blocking of bacterial DNA replication by binding itself to an enzyme called DNA gyrase, which allows the untwisting required to replicate one DNA double helix into two [1]. Gatifloxacin and other fluoroquinolones are effective against a broad spectrum of bacteria that may cause ocular infections in humans including endophthalmitis and conjunctivitis [2]. Melo et al found that gatifloxacin was effective against a range of both Gram positive and Gram negative microorganisms including anaerobes when tested in vitro. Unfortunately it is associated with systemic toxicity in humans. Dhavaleshwar et al reported a case of Moxifloxacin induced Steven Johnson Syndrome in 18 year old female patient treated for bacterial conjunctivitis [3]. Maria et al reported a case of other Fluoroquinolone - Levofloxacin induced Steven Johnson Syndrome/ Toxic epidermal necrolysis after the treatment for pneumonia [4].

PATIENT INFORMATION

A 65-year-old male patient presented in the General medicine OP department with the complaints of pain associated with mouth ulcer since 1 week. On probing further history of instillation of Gatifloxacin eye drops, 3 times daily for 3 subsequent days for the treatment of Bacterial conjunctivitis were elicited. The initial blister appeared after application of the eye drops in second day. Blisters progressed more by the third day and patient stopped medication, sought care from other tertiary care hospitals, left inappropriately identified as drug induced. Initially appeared blisters on the upper part of the lips and below the nose were popped by the patient and later on progressed into the ulcerative lesions.

CLINICAL FINDINGS

On examination, patient was conscious and oriented, per abdomen soft and non-tender, ulcerative lesions over the upper and lower part of the lips leading to upper palate and lower tongue. Oral ulcers noted extending from oral fissure as multiple erosions

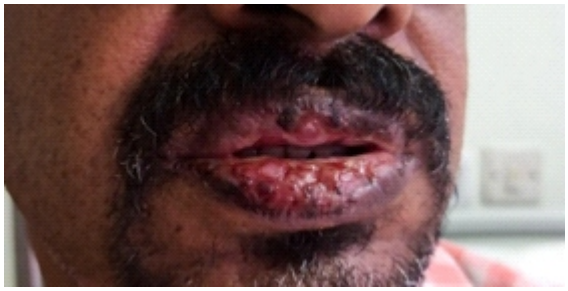

Fig. 1 : Steven Johnson Syndrome- ulcer lesions in upper and lower lips of the patient

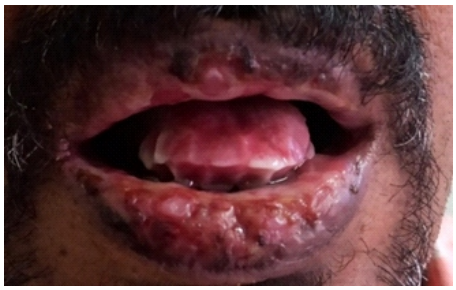

Fig. 2 : Skin peeling ulcerative lesions over tongue extent to upper palate and lower tongue.

with sloughed mucosa covered by a whitish membrane over buccal mucosa. Sloughing and ulceration of lips along with severe inflammatory oedema was present. Patient was unable to feed even in liquid form.

TIMELINE

Patient care was organized at appropriate timing after the patient was admitted in the hospital with antibiotics and anti-inflammatory medications from the first day of admission.

Diagnostic Assessment

Provisional Diagnosis made as Drug induced Hypersensitivity with main diagnosis as Gatifloxacin induced Erythema multiforme minor. Blood laboratory parameters of the patient were evaluated on daily basis for assessing the response of the patient to the treatment given.

THERAPUTIC INTERVENTIONS

With provisional diagnosis as Stevens - Johnson Syndrome-: Drug induced Hypersensitivity (Erythema multiforme minor) patient was started on following treatment:

CORTICOSTEROIDS: Inj. Hydrocortisone 100 mg as stat medication followed by Inj Hydrocortisone 100 mg every 8th hourly. On Day 3 Inj. Hydrocortisone dose deescalated to 100 mg twice daily, later on changed to Tab. methyl prednisolone 8 mg twice daily for 3 days and after discharge to Tab. methyl prednisolone 4mg twice daily for 2 days , once daily for 2 days and 2mg twice for 2 days.

ANTIBIOTICS: Inj. Meropenem 1g intravenously twice daily was added and switched over to Tab. Faropenem 300mg twice daily for 4 days. Inj Metronidazole 500mg twice daily for 4 days.

Table 1 : The Laboratory findings of the patient

LABORATORY VALUES	Day 1	Day 2	Day 3	Day 4	Day 5
Total count(cells/mm3)	13,090	12,870	11,940	10,800	15,990
C reactive protein(mg/L)	62.7	28.4	7.2	16.8	8.5
ESR(mm/hr)	43	35	18	14	16

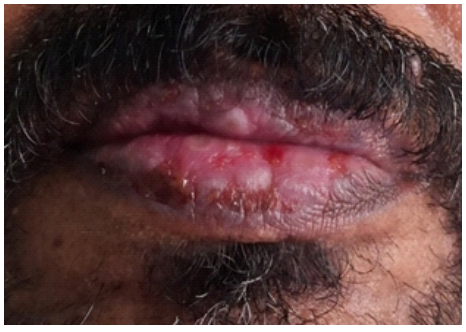

Fig. 3 : Decreased ulcer lesions over upper and lower lips.

After treatment.

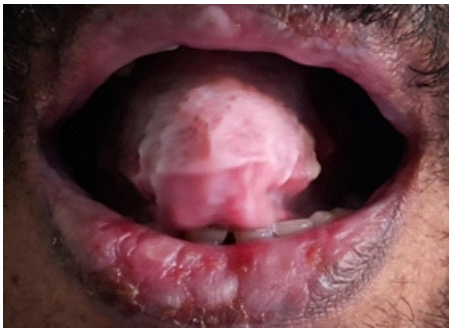

Fig. 4 : Healing lesions over the tongue

After treatment.

TOPICAL APPLICANTS: Triamcinolone acetonide ointment and Clotrimazole mouth paint were prescribed for topical application on the affected area from the day of admission and continued after discharge for 5 days.

VITAMIN SUPPLEMENTS: Tab. Folic acid 5mg once daily and Tab. Supradyn containing multivitamins were supplemented.

INJECTION NOVORAPID: Short acting insulin were added for diabetes control later on changed to Tab. Torglip (Vildagliptin) 50 mg once daily.

FOLLOW UP AND OUTCOMES

The outcomes were assessed by the improvement of the condition in the patient and laboratory parameters. The patient was asked for follow up after 10 days of discharge with CBC, FBS, ESR and CRP reports**.**

DISCUSSION

Erythema multiforme (EM) is an acute, self-limited and sometimes recurring skin condition that is considered to be a type IV hypersensitivity reaction associated with certain infections, medications and other various triggers. Erythema multiforme may be present within a wide spectrum of severity. Erythema multiforme minor represents a localized eruption of the skin with minimal or no mucosal involvement. The papules evolve into pathognomonic target or iris lesions that appear within a 72-hour period and begin on the extremities Erythema multiforme major is a more severe, potentially life-threatening disorder. One or more mucous membranes are involved and up to 10% of body area may have epidermal detachment [5]. The strength of this report is unexpected hypersensitivity response to just topical application of few drops of gatifloxacin.

A careful history of use of offending drugs with clinical examination for skin and mucous membrane involvement should raise high suspicion for the condition. Although the recovery in our case was quite satisfactory long-term follow-up is warranted to look into complications and appropriate management. Antibiotics, even when used in the topical dosage form, can cause serious systemic problems like SJS as reported in this. Therefore, over the counter use of the medication should not be encouraged. Steven Johnson Syndrome can be fatal if not diagnosed and treated accordingly at the due time in accordance with remedial right medications.

PATIENT PERSPECTIVE

Patient became far better and was satisfied with the treatment given as his ulcers were healed.

INFORMED CONSENT

The case report was done after getting informed consent from the patient. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity.

CONCLUSION

Though the systemic use of Gatifloxacin was banned, it is used topically to treat bacterial infections. This case report provides strong evidence linking the use of gatifloxacin to the development of Steven Johnson Syndrome (SJS). The patient's clinical presentation, temporal relationship between drug administration and symptom onset, and resolution of symptoms upon discontinuation of the medication support the causal association. Healthcare providers should be aware of this potential adverse reaction and consider alternative antibiotics in patients at higher risk for SJS when prescribing gatifloxacin.

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