IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 20, Issue 6 Ser.14 (June. 2021), PP 49-52
www.iosrjournals.org

A Case Report: Levofloxacin Induced Steven Johnson Syndrome

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Abstract:
An adverse drug reaction (ADRs) is an unwanted or harmful reaction experienced following the administration of a drug or combination of drugs. Adverse drug reactions remain a challenge in modern healthcare. They account for about 5% of all hospital admission and cause death in approximately 0.01% patients. These may vary from mild, moderate to severe or lethal reactions. We report a case of Levofloxacin induced Steven Johnson Syndrome in a 70 year old male patient admitted in emergency ward of our college.
Keywords: *Levofloxacin, Drug Induced Steven Johnson Syndrome, Fluoroquinolones, Adverse Drug Reaction.*

Date of Submission: 17-06-2021 Date of Acceptance: 02-07-2021

I. Introduction

The World Health Organization defines Adverse Drug Reaction (ADR) or Adverse reaction "As a response to a drug, which is noxious and unintended, which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of a disease or for the modification of physiological functions."[1] World statistics reveal that 0.3- 7 % of the hospital admissions were attributed to adverse drug reaction. These may vary from mild rashes to severe reactions such as Steven Johnson Syndrome. 5-8 % of hospitalized patients develop serious Adverse Drug Reaction. There are wide ranges of factors which can influence ADR development like patient related factors, social factors, drug related factors and disease related factors. [2]

Steven Johnson Syndrome is a severe life threatening mucocutaneous syndrome caused by drugs like antimicrobials, antiepileptic and analgesics.

Levofloxacin is the active levo(s) isomer of Ofloxacin having improved activity against Streptococcus pneumoniae and some other gram-positive and gram-negative bacteria. The primary indication of Levofloxacin is community acquired pneumonia and exacerbations of chronic bronchitis. It inhibits the bacterial enzyme DNA gyrase which is required for DNA replication and transcription. [3]

During ADR monitoring we reported a typical case of Steven Johnson Syndrome following the administration of Levofloxacin.

II. Case Report

A 70 year old man weighing 68 kgs was admitted to the emergency department at our teaching Hospital with chief complaints of crusting and ulcer over oral mucosa since past two days and rashes over trunk and redness over face and high grade fever since one day.

The patient was apparently asymptomatic three days back when he developed complaints of cough for which he was prescribed tablet Levofloxacin 500mg once a day for three days.

From second day of oral administration of drug he developed crusting and ulcer over oral mucosa and lips which was acute in onset and gradually involved entire oral mucosa followed by difficulty in swallowing. The lesion was painful with bleeding while eating, so his appetite was reduced. After that he observed rashes which appeared as red, raised lesions beginning from the face and progressed over trunk and then involving middle side of bilateral thigh. Figure 1 shows the rashes on the trunk. These rashes were painful and accompanied by itching all over it. Third day onward he developed hyperpyrexia. Finally, he was admitted to the emergency ward of our institute in the above mentioned condition.

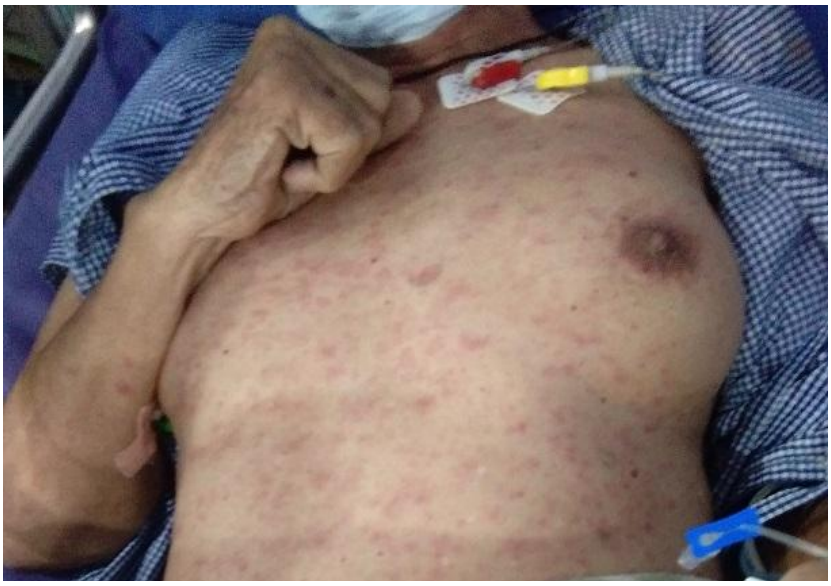

Fig. 1

On physical examination, the patient was well oriented with time, place and person and had lesions as described earlier. Intraoral examination revealed ulcerations over entire upper and lower lips, buccal mucosa, tongue and palate and were tender. Figure 2 and 3 shows ulcers on the upper and lower lips, buccal mucosa and tongue. Consent for using the photographs of patients was taken.

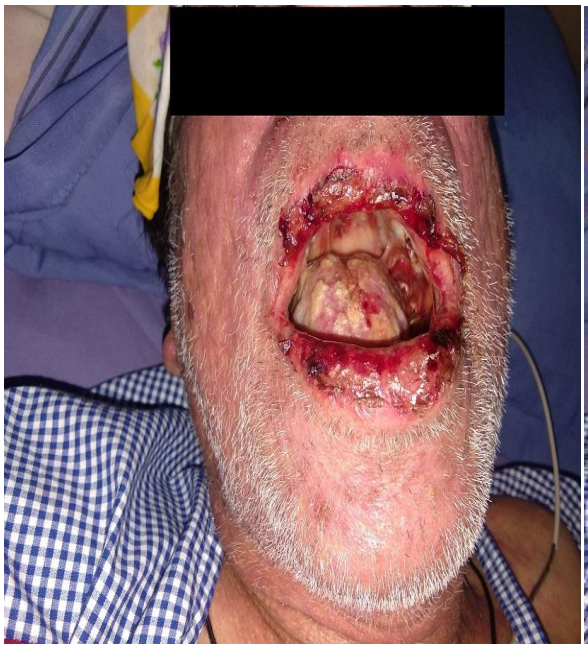

Fig. 2

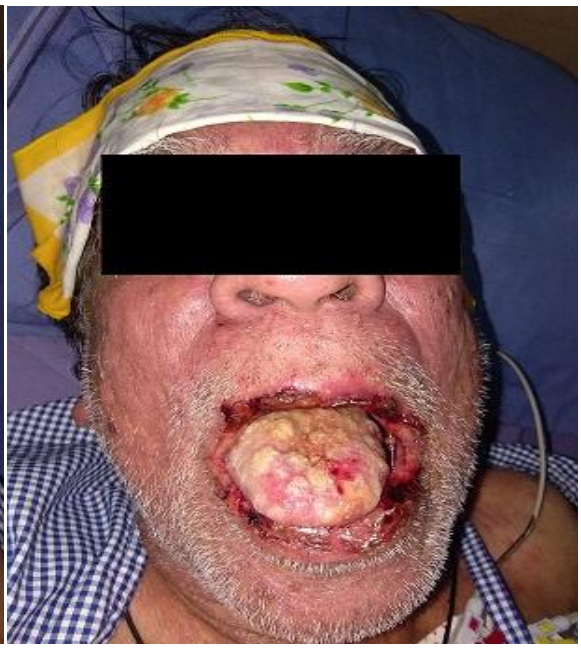

Fig. 3

On general examination, blood pressure was 132/72 mm/Hg, pulse – 90 beats/min, temperature – 102.9^0 F, respiratory rate – 20/min, chest auscultation and abdominal palpitation did not reveal any significant finding. The following investigations were done - HB – 10mm/dl, TLC – 8200/mm3, platelets – 1.4 lakh, bleeding time and clotting time were normal and Liver function test was within normal limits.

The Patient also had a medical history of Herpes Zoster Ophthalmicus two months back for which he underwent complete treatment. Now ophthalmic examination shows conjunctivitis, pain in left eye and discharge since past two days.

The patient was immediately admitted with diagnosis of drug induced Steven Johnson Syndrome with post herpetic neuralgia and Tablet Levofloxacin was immediately stopped. Patient was administered with intravenous fluids (50 ml/hour), Tablet Levocetrizine 5 mg once a day, Table Acyclovir 400 mg thrice a day, Intravenous Sumol 100 ml thrice a day, Intravenous dexamethasone 0.5 thrice a day.

Oral ulcers are being treated with Orahelp ointment local application thrice a day before meal, Oraways ointment local application thrice a day after meals and Chlorhexidine mouthwash thrice a day. For eye lesion Refresh tears eye drops was prescribed. T-bact ointment local application twice a day is being applied gently over the skin followed by strict aseptic measures.

Adverse Drug Reactions (ADRs) are a major cause of morbidity, hospital admissions and even death. Hence it is essential to recognize ADRs and to establish a causal relationship between the drug and the adverse event. It is desirable that ADRs should be objectively assessed and presented based on an acceptable "Probability Scale". Many causality methods have been proposed to assess the relationship between a drug and an adverse event. The causality assessment system proposed by the World Health Organization Collaborating Centre for International drug monitoring, the Uppsala Monitoring Centre(WHO-UMC) and Naranjo Probability Scale are generally accepted and most widely used methods for causality assessment in clinical practice as they offer simple methodology.[4,5] Causality assessment using Naranjo's algorithm categorized the adverse drug reaction as probable/likely (score = 5) and by WHO scale was also classified to be probable.

Patient started showing improvement from second day of treatment, had blood pressure – 120/70 mm/Hg, pulse – 90 beats/min, temperature – 99^0 F, respiratory rate – 14/min. After 7 days of treatment, temperature was 97.4^0 F and the patient was recovering well.

We reported the ADR in vigiflow for further assessment by National Coordination Center (NCC) under Pharmacovigilance programme of India (PVPI), Indian Pharmacopoeia Commission (IPC) Ghaziabad.

III. Discussion

Steven Johnson Syndrome is a life threatening immune complex mediated hypersensitivity reaction which mainly involves skin and mucous membrane. Steven Johnson Syndrome is generally induced by the drugs like Anticonvulsants, Sulfonamides, Nonsteroidal anti- inflammatory drugs, Corticosteroids, Imidazole antifungal, Cephalosporins, Allopurinol, broad-spectrum bactericidal agents, Quinolones and Fluoroquinolones. The manifestations include blisters on skin, facial swelling and pigmentation. Its more severe form is called toxic epidermal necrolysis (TEN). [6]

It is believed that drugs are the main cause of Steven Johnson Syndrome(50 to 80% of cases) and Toxic epidermal necrolysis(around 80%), although these diseases can also be triggered by infections and malignancies, while drugs and cancer are more associated with adult patients, infections are the leading cause in children.[7]

Some people with Steven Johnson Syndrome have a genetic predisposition which increases their risk of developing the condition in response to triggering factors such as medications. The genetic variation most strongly associated with Steven Johnson Syndrome occurs in the HLA-B gene. This gene is part of a family of genes called the human leukocyte antigen (HLA) complex. This complex of genes helps the immune system distinguish the body's own proteins from proteins made by foreign invaders (such as viruses and bacteria). Variations in several other HLA and non HLA genes have also been studied as possible risk factors for Steven Johnson Syndrome. [8, 9]

Steven Johnson Syndrome can affect any age, either sex and all races, although it is more common in older people and women. It is much more likely to occur in human immunodeficiency virus (HIV), viral infections, genetic factors, vaccination, graft versus host disease, malignancy, and idiopathic.

The initial step for Steven Johnson Syndrome/ Toxic epidermal necrolysis may be interaction/binding of a drug associated antigen or metabolite with the major histocompatibility complex (MHC) type 1 or cellular peptide to form an immunogenic compound. It is T- cell mediated. CD8+ cells are present in blister fluid and may induce keratinocyte apoptosis. CD40 ligand cells are also present and may induce release of TNF- alpha, nitrous oxide, interleukin 8(IL-8) and cell adhesion antibodies. TNF- alpha also induces apoptosis. Both Th1 and Th2 cytokines are present. Other cells include macrophages, neutrophils, and natural killer (NK) cells. The pharmacologic interaction of drugs with the immune system could result in binding of the responsible drug to MHC-1 and the T cell receptor. [10, 11]

Levofloxacin is second generation Fluoroquinolones. Fluoroquinolones are bactericidal in nature. Levofloxacin is also used in sinusitis, pyelonephritis, prostatitis and other urinary tract infections and skin and soft tissue infections. Its adverse events reported are nausea, vomiting, diarrhea, headache, constipation, dizziness, abdominal pain, abdominal gas, itching, rash, hives, difficulty sleeping, anaphylaxis (shock) and dyspepsia.

The Fluoroquinolones are also associated with less frequently reported, but potentially serious adverse events. These events include seizures, tendonitis, allergic reactions, disturbances in glucose metabolism, hepatotoxicity, peripheral neuropathy, Clostridium difficile-associated diarrhea and Photosensitivity/Phototoxicity. [12, 13]

There were few published reports of Levofloxacin induced Steven Johnson Syndrome in India. Gajjar K et al. reported in 2018 a cross sensitivity reaction between Levofloxacin and Ciprofloxacin which presented as

toxic epidermal necrolysis. [14] Verma SK et al. reported in 2013 a case of hypersensitivity reaction with Levofloxacin and Furazolidone which presented as toxic epidermal necrolysis. [15]
These cases were more severe and progressed to toxic epidermal necrolysis.
We are presenting this case in north Indian population and only depicts Levofloxacin induced Steven Johnson Syndrome which is not progressed to toxic epidermal necrolysis. It will help the physicians in being cautious while prescribing Levofloxacin. They should take a proper history and educate the patient for being vigilant about these side effects.

IV. Conclusion

This was a case of Levofloxacin induced Steven Johnson Syndrome. The main purpose of reporting this Adverse Drug Reaction is to create awareness so that Levofloxacin re-administration can be avoided in patients with a previous history of Steven Johnson Syndrome or allergic skin reaction to Levofloxacin by obtaining an accurate medical history.

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Acknowledgement: - None

Dr. Shruti Srivastava (BDS), et. al. "A Case Report: Levofloxacin Induced Steven Johnson Syndrome." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 20(06), 2021, pp. 49-52.