A Case Report on Etoricoxib Induced Stevens Johnson Syndrome

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ABSTRACT

Etoricoxib is a selective cyclo-oxygenase enzyme-2 (COX-2) inhibitor which is majorly indicated in the treatment of inflammatory disorders such as rheumatoid arthritis, osteoarthritis and gout. Etoricoxib selectively inhibits COX-2 thereby inhibiting the conversion of arachidonic acid to prostaglandins (PG's). Stevens–Johnson Syndrome (SJS) is a rare, life threatening hypersensitivity reaction that predominantly affects skin and mucous membrane which is characterised by extensive epidermal necrosis. Some of the medications which are associated with the development of Stevens Johnson syndrome include xanthine oxidase inhibitors such as allopurinol, anti-epileptic medications such as carbamazepine, lamotrigine, phenytoin and Non-Steroidal Anti-Inflammatory Drugs (NSAID's). In this case report, we summarize regarding a patient who developed SJS after usage of etoricoxib that was managed by cessation of the offending agent and symptomatic treatment concomitant with supportive care.

Key words: Cyclo-Oxygenase enzyme-2 (COX-2), Prostaglandins (PGs), Hypersensitivity, Necrosis, Non-Steroidal Anti-Inflammatory Drugs (NSAID's).

INTRODUCTION

Stevens–Johnson Syndrome (SJS) is a rare, life threatening hypersensitivity reaction that predominantly affects skin and mucous membrane which is characterised by extensive epidermal necrosis. According to Gell and coombs classification of hypersensitivity reactions, SJS is classified as type-IV (subtype C) hypersensitivity reaction. The first case of SJS was reported by two American paediatricians Albert Mason Stevens and Frank Chambliss Johnson in 1922. The incidence rate of SJS is 7 cases per million population per year. In most of the cases SJS is usually triggered by an adverse reaction to a medication. Some of the medications which are associated with the development of Stevens Johnson syndrome include Xanthine oxidase inhibitors such as allopurinol, Anti-epileptics such as carbamazepine, lamotrigine, phenytoin, Sulphonamide antibiotics such as sulfamethoxazole and NSAID's (Non-Steroidal Anti-Inflammatory Drugs). Stevens-Johnson syndrome can also be caused by infections such as herpes-simplex virus, Epstein-Barr virus. Rarely, bacterial infections can also cause Stevens-Johnson syndrome. Typical signs and symptoms of SJS include fever, A red or purple skin rash, blisters on skin and the mucous membranes of mouth, nose, eyes and genitals, shedding of skin within days after blisters form, sore throat, fatigue, cough, burning eyes. Genetic predisposition of certain Human Leukocyte Antigens (HLA) has been linked with increased likelihood for development of SJS. There is no specific treatment protocol is for Stevens-Johnson syndrome and therefore most of the patients are provided with supportive care and symptomatic treatment and usually involves identification and cessation of offending agent. The major components involved in pathological development of SJS include immunological reactions, reactive drug metabolites and genetical aspects.[1]

Etoricoxib is a selective COX-2 (Cyclo-Oxygenase enzyme-2) inhibitor which is majorly indicated in the treatment of inflammatory disorders such as rheumatoid arthritis, osteoarthritis and gout. This

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drug was patented in 1996 and approved for medical use in 2002. Etoricoxib selectively inhibits cyclo-oxygenase enzyme-2. Cyclo-oxygenase is involved in the conversion of arachidonic acid to prostaglandins (PG's). Prostaglandins play a major role in generation of inflammatory response. Drug safety reports and few case reports suggest that etoricoxib is associated with the development of severe cutaneous adverse reactions (SCARs) such as Stevens–Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN) and Erythema multiforme.[2]

CASE REPORT

A 45-year-old female patient was admitted in the emergency department, Malla Reddy hospital, Suraram with chief complaints of rash, eruptions on skin which are associated with itching, black plaques were present over both upper limbs, minor lesions all over the body and redness is present around the lesions. Patient was apparently asymptomatic 20 days back and then she developed pain in the right knee and is advised to take etoricoxib. Following the intake of etoricoxib for 15 days, patient developed the above symptoms. Patient had a past medical history of hypertension since 3 years and on medication. On examination her vitals were found to be normal. Fixed drug eruption was suspected based on her symptoms. Viral serology for hepatitis B and C was found negative. Complete blood picture was found to be normal. Other biochemical investigations such as random blood sugar, blood urea and serum creatinine were also found to be normal. Absolute eosinophil count was 450 cells/mm^3. CRP (C Reactive protein) was found to be 2.4mg/dl. ESR (Erythrocyte sedimentation rate) was observed to be 5mm/hr. upon local examination multiple mucosal erosions and vaginal mucosal erosions were present. Conjunctival congestion was present. Multiple erythematous to polymorphic plaques were present all over the arms, back of trunk, thighs and palms. Lacrimal apparatus showed mucoid discharge with pus. Erosions and lesions were also present on the lips. Based on the local examination and laboratory investigations the patient was finally diagnosed with etoricoxib induced Stevens Johnson Syndrome.

The physician advised the following medications [Table 1] following cessation of offending agent simultaneously with supportive care. Patient was discharged after 9 days and is advised with following discharge medications which include tab Atarax, mucopain gel, linical lotion, betadine gargle and Fucidin cream.

Table 1: Medication chart.

Brand Name	Generic Name	Dose	Frequency
Tablet Atarax	Hydroxyzine	10 mg	Stat
Injection Augmentin	Amoxycillin and potassium clavulanate	1.2 gm	BD
Lactocalamine lotion	Glycerine, zinc oxide and kaolin	L/A	SOS
Tablet Xyzal	Levocetirizine	5 mg	OD
Mucopain gel	Benzocaine	L/A	BD
Vigamox drops	Moxifloxacin	5 ml	QID
TESS cream	Triamcinolone	L/A	SOS

DISCUSSION

In recent years, adverse drug reactions (ADRs) are identified as the major public health concern and they are considered to be one of the leading causes of morbidity and mortality among hospitalised patients. Proper patient counselling and effective monitoring of ADRs is required as there is increased usage of pain killer medications especially NSAID's.

SJS is a life-threatening condition which can be fatal if treatment is not initiated in appropriate time and can also lead to complications such as shock, multi organ failure and kidney damage.

The international classification of SJS/TEN is based on body surface area involvement.

Condition	Body surface area involved
Stevens Johnson Syndrome	Less than 10%
Overlapping Stevens Johnson syndrome or Toxic Epidermal Necrolysis	10-30%
Toxic Epidermal Necrolysis	More than 30%

The exact pathogenesis of SJS is unknown but few studies revealed that it is a T cell mediated cytotoxic reaction to drug antigen in keratinocytes which leads to massive destruction of epidermis leading to blister formation.

ALDEN (Algorithm of drug causality for epidermal necrolysis), an algorithm which is a specific causality assessment algorithm for SJS/TEN, shows that the ADR is probable with score of 5. The ADR was of moderate severity of level 4 as per the Hartwig's Severity Assessment Scale and was not preventable according to Modified Schumock and Thronton criteria for preventability of ADR.[3-5]

CONCLUSION

The crucial step in the management of the SJS is to identify the offending agent by temporal relationship.

Pharmacists should alert the patients about the possible ADRs associated with usage of etoricoxib and other commonly prescribed NSAID's. Health Care Professionals must counsel the patients and advise them to report as soon as possible if they experience any unwanted side effects due to medications especially when prescribed with high risk medications. This also suggests that clinical pharmacist plays a key role in Health care sector by improving patient education and enhancing patient care.

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CONFLICT OF INTREST

The authors declare that they have no conflict of interest.

ABBREVIATIONS

CRP: C Reactive protein; **ESR:** Erythrocyte sedimentation rate; **COX:** Cyclo-Oxygenase; **PG:** Prostaglandins; **SJS:** Stevens Johnson Syndrome; **ADR:** Adverse Drug Reaction; **TEN:** Toxic Epidermal Necrolysis; **ALDEN:** Algorithm of drug causality for epidermal necrolysis.

SUMMARY

In summary, this is a case of a patient who developed SJS after usage of etoricoxib that was managed by cessation of the offending agent and symptomatic treatment concomitant with supportive care.

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