Case Report

FATAL OUTCOME OF STEVENS JOHNSON SYNDROME (SJS) ASSOCIATED WITH AZITHROMYCIN

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SUMMARY

Most of the medical practitioner's are under the impression that Stevens Johnson Syndrome (SJS) is an uncommon life threatening drug reaction. In fact it is not as rare a disorder as we are led to believe. Stevens Johnson Foundation claims that they come to know of 15 new cases a week and that is only people with internet access. In Bangladesh the real burden is never estimated as information on monitoring and reporting of adverse drug reactions are not available. Stevens Johnson Syndrome is an immune complex mediated idiosyncratic systemic hypersensitivity reaction that may be triggered by medications, viral, bacterial, fungal infection and malignancies. Recent reports link SJS to the use of drugs rather then other etiologies. Here we report a case of SJS with fatal outcome which is probably the first case encountered in Bangladesh induced by Azithromycin.

KEY WORDS: Stevens Johnson Syndrome, Drug Reactions.

Pak J Med Sci April - June 2008 (Part-II) Vol. 24 No. 3 455-457

How to cite this article:

Nur J, Chowdhury FR, Nazmul Ahasan HAM, Alam B. Fatal outcome of Stevens Johnson Syndrome (SJS) associated with Azithromycin. Pak J Med Sci 2008;24(3):455-7.

INTRODUCTION

A women of 40 years came to Dhaka Medical College Hospital on 14thAugust 2007 with agonizing vesiculobullous eruptions all over her body and remittent fever. She had had a total abdominal hysterectomy on 19th July 2007 due to chronic cervicitis. She had been on intravenous ceftriaxone, diclofenac and ranitidine during her immediate post-operative period which had been switched three days later to cefixime for four days. She was also found to be prescribed Azithromycin (AZM) for seven days during her discharge on 26th July 2007. She took the drug as an outpatient and claimed of having been in good health except a mild attack of fever, headache and malaise on 1st August 2007. Four days later, she found herself with red flat rashes on her entire body along with red and swollen eyes. She also had high fever. By the following days the rashes evolved to vesicular and bullous form and blisters filled her mouth making her unable to take any food.

On arrival we found her with florid form of erythematous bullae with blisters and crust formation. She had conjunctival injection with mucopurulent discharge, many oral and pharyngeal ulcers, healthy anogenital mucosa with normal urine and stool color. She was toxic,

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* Received for Publication: December 19, 2007
* Revision Reiceved: April 16, 2008
* Revision Accpeted : May 2, 2008

mildly anaemic; temperature was 103^0F. Vital signs and systemic examination revealed normal findings. Area of denuded skin was 3% and SCORTEN score[1] was only one. Laboratory investigations showed WBC count of 8.9K/cmm with normal differential count. ESR was 35mm in first hour. Urine analysis, serum electrolytes, Anti-nuclear antibody, liver and renal function tests were within normal limit. Antibodies against Herpes simplex virus, mycoplasma pneumoniae and skin biopsy were not done.

We diagnosed her as having Stevens Johnson Syndrome (SJS) evaluating history, nature and distribution of lesions along with lack of other potential confounding factors. She completed the course of AZM before taking admission and had been no longer on AZM. Intravenous dexamethasone and intramuscular pheniramine maleate were started along with all other supportive managements including diclofenac for pain relief, ranitidine to prevent stress ulcer, intravenous ceftriaxone, antibiotic eye drop and ointment, povidone iodine mouth wash etc. We applied steroid here as a life saving tool having no facilities for intravenous immunoglobulin (IVIg) therapy which had been proved to be effective in some cases of SJS with AZM.[2,3]

Her general condition improved on the next day and she felt well enough during subsequent five hospital days with continuation of same managements. Unfortunately on 19th August she was found distressed, dyspnoeic and dehydrated. The rashes looked more aggressive with haematoma formation and inflamed eyes showed sub-conjunctival hemorrhage. In spite of resuscitation her condition deteriorated with appearance of widespread crackles and rhonchi all over her lung fields. High fever continued and despite all efforts she too expired on 21st August, 2007.

DISCUSSION

Most of the medical practitioners are under the impression that SJS is an uncommon life threatening drug reaction with the incidence of 1.2-6 per million patient-years and a mortality rate of 5%.[4] In fact it is not as rare a disorder as we are led to believe. SJS Foundation claims of learning 15 new cases a week and that is only people with internet access.[5]In Bangladesh unfortunately where over-prescription, polypharmacy and self medication are alarmingly common practice, it is one of the most under-reported conditions and the real burden is never estimated. Ironically, SJS remains as puzzling a disorder as it was 85 years ago, when discovered by Stevens and Johnson[6] Diagnosis is still based on the antecedent drug history and the hallmark of lesions on at least two mucosal surfaces.[7] No laboratory study except skin biopsy can help to establish the diagnosis. A drug etiology for SJS is easy to postulate but difficult to prove because of lack of reliable tests. Consideration must be given to the likelihood of a particular drug to cause the syndrome when multiple drugs are anticipated.[8] To distinguish the culprit drug among several suspected drugs, skillful history regarding timing of administration and its temporal relationship to the onset of syndrome must be evaluated.[8] The sensitivity and specificity of Patch test,[9] in vitro lymphocyte tests[9] are variable. Although rechallenge tests would provide convincing evidence such testing is not feasible for ethical reasons. After prompt recognition and discontinuation of responsible drug treatment is merely symptomatic. Therapeutic trends currently being practiced have long been argued. Efficacy of drugs described in different case reports and studies is difficult to evaluate: IVIg, steroids, cyclosporine, cyclophosphamide, pentoxyfillin, thalidomide, plasmapharesis, haemodialysis all have been tried reaching no conclusive option.[10] Recently IVIg has shown some promises in both treatment[11] and prophylaxis.[12]

Here we have convicted AZM to be the offender; because, the patient took diclofenac and ranitidine every now and then as a pain reliever (for several times) before undergoing surgery and she denied any previous drug reaction attack. It is a possibility that the rashes might have resulted from cefixime as the SCAR(severe cutaneous adverse reaction) for cephalosporins is 63% compared to 44% for AZM.[13] We know, by definition drug eruptions

occur 1-3 weeks after exposure and recurrences are more rapid and severe.[7] In our case the close temporal relationship points towards AZM. Moreover, she received cephalosporin (ceftriaxone) upon admission and during her previous hospital stay. But no additional symptom and sign (ceftriaxone, cefixime) appeared during this re exposure rather her condition improved.

The paradox drawing our attention is the death of the patient in spite of having a SCORTEN score of one during admission along with transient improvement after starting treatment. It might be due to the fact that the patient failed to discontinue the drug early and took two unnecessary doses adding insult to the injury. Also, the longer half-life of AZM might have contributed to her deterioration and delayed development of pulmonary complications & circulatory collapse during hospital stay. It has been reported that timely withdrawal of the causative drug may reduce the risk of death by 30% per day particularly drugs with short half life[14] and the mortality rate is much higher in SJS with pulmonary complications.[15] Above all, the long debated role of steroid in inviting secondary infection and masking the early sign symptoms of sepsis is a great concern. Although steroid is found beneficial in most of the cases and is widely used in our country.

SJS can kill or severely disable previously healthy people of all ages. Any medication can invite this monster and its potential cannot be anticipated or prevented. The reported case is probably the first case encountered in Bangladesh induced by AZM. List of drugs implicated to cause it is increasing day by day and till now the most invaluable tool in minimizing its long term effects is early medical attention. So, great commitments are required from drug regulating authority, drug manufacturer and health care professionals. Parents should not rush to give their kids medication for minor illness, pharmaceutical companies should supply all necessary information with every drug and physicians should consider alternative therapies with substantially lower risk.

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