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NIMESULIDE INDUCED STEVENS-JOHNSON SYNDROME – AN ADVERSE DRUG REACTION

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ABSTRACT

Adverse drug reaction is one of the serious clinical issues of concern in the modern-day pharmacotherapy, there forth imposing a threat to patient wellbeing. Stevens-Johnson Syndrome is a rare, serious and potentially life-threatening cutaneous reaction, primarily involving skin and muco cutaneous ulcerations, notably caused by drug intake and other intermittent infections. This case substantially highlights the importance of Nimeusulide as the primary agent causing Stevens-Johnson Syndrome hence, its use should be judiciously monitored in order to prevent such fatal reactions. We report a case of 27-year-old female presented with vesicular rupture in eye, oral cavity, throat, and genital area associated with burning micturition, odynophagia and pus discharge. On the whole, comprehensive clinical and laboratory findings confirmed the diagnosis as Nimesulide induced Stevens-Johnson Syndrome.

KEYWORDS: Stevens-Johnson Syndrome (SJS), Nimesulide, Naranjo's ADR probability Scale.

INTRODUCTION

Adverse drug reaction is considered as one of the serious intimidating issues arising in the modern-day pharmacotherapy, thereforth imposing a threat to patient wellbeing.[1] Stevens-Johnson Syndrome is considerably a rare, serious and potentially life-threatening reaction. "A new eruptive fever with stomatitis and opthalmia".[1,2] In the year 1922, Albert Mason Stevens and Frank Chambliss Johnson coined the phrase Stevens-Johnson Syndrome.[3] Additionally, mucosal involvement is the characteristic feature present in more than 90% of cases, along with epidermal detachment of<10% of Total Body surface area.[4] Other than mucosal involvement, the most frequently affected organs are liver, kidney, and lungs.[5] Moreover,

most commonly implicated drugs causing SJS are antibacterial (sulphonamides), NSAIDS (Paracetamol, Nimesulide), cephalosporin, anticonvulsants (phenytoin, phenobarbitone, carbamazepine), and anti-gout drugs (allopurinol).[6,7] We report a case of Nimesulide induced Stevens-Johnson Syndrome wherein affecting lips, eyes, throat and external genital areas.

CASE REPORT

A 27 year old female presented to the emergency department of our hospital with complaints of odynophagia, vesicular rupture, initially in the eye then proceeding to oral cavity, throat, and external genital area for 4 days, along with fever not associated with chills and rigors with no diurnal variations. She also had a history of burning micturition consequently with the above symptoms. On examination, her features looked dull as shown in Figure 1; vitals were stable. Similarly, oral examination revealed itchy, painful lesions on the lips, diffuse fissures, erosions, erythema with crusting and hyperpigmentation on the lips accompanied with congestion of oral mucosa. Furthermore, ocular examination exhibited watering of bilateral of both eyes with collection of whitish material in the medial canthus was noted. Erythematous papules were seen on bilateral external of hands, dorsum of foot and palms; few target lesions were present on palms and external genital areas.

After further inquiry, the patient revealed she had a history of intake of Nimesulide tablet as an over the counter drug for headache six days back prior to admission. On further investigation, she had no history of any previous drug allergies. Various laboratory investigations were performed which includes Complete blood picture, serum electrolytes, and viral markers. In the complete blood picture report, Haemoglobin level was found to be low (10.4g/dl), MCH (20.4), MCV (64.7), HCT (33). Urine levels were normal. HIV I and II, HBsAg, and HCV test was non-reactive.

The patient's drug history, significant clinical examination and laboratory findings lead to the confirmatory diagnosis as Nimesulide induced Stevens-Johnson Syndrome. Appropriate Stepwise approach for management of the disease was followed; thereby the treatment included systemic dexamethasone, twice a day for three days, gradually tapered off to once a day wherein cephalosporin were added as a prophylaxis for super infection. Topical steroids and mouthwash were used for oral lesions. Eye drops for ocular lesions; normal saline compressions were carried out for lips and eyes. The discharge medications included Omnacortil. 10 mg for a course of 9 days, with the pattern of thrice a day for three days,

twice a day for three days and once a day for three days. The continuation of topical steroids was also advised. At follow up she was symptomatically better and was able to tolerate oral fluids.

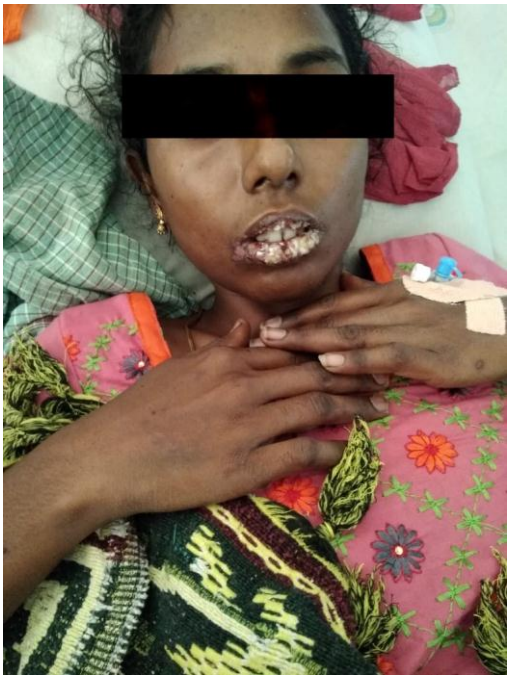

Figure 1: Patient with application of an ointment for the lesion on the lips.

DISCUSSION

Nimesulide, a selective cycle-oxygenase inhibitor (COX2), is an anti-inflammatory agent which is available as an over the counter drug in India.[8,9] Due to a relatively short plasma life, the incidence of sever gastrointestinal and renal toxicity is low. Henceforth, unprecedented drug usage leads to various skin reactions such as erythema, urticaria and Stevens-Johnson Syndrome.[9] Generally, it is often drug induced, or idiopathic despite of its vast etiological factors fever and flu are the first marks of Stevens-Johnson Syndrome, accompanied by erythematous and cutaneous macules, filled with mucous, presenting a picture of a painful lesion.

The extent of epidermal detachment is less than 10%, widespread over the body, with atypical targets. The involvement of the Stevens-Johnson Syndrome can vary from confined spaces such as mouth to organ systems such as respiratory, gastrointestinal in severe cases.[11]

The etiology of SJS is vast; it can range from various infections such as Herpes simplex virus, Mycoplasma pneumoniae, and upper respiratory infections to radiation therapy and environmental chemicals. However, for efficient diagnosis of SJS, both clinical symptoms

and histopathological findings are taken into consideration. Vivid presentation of erythema and macules on the skin followed by blisters is an indication of SJS syndrome. Electrolytes, liver function tests, blood urea nitrogen, electrolyte imbalance, complete blood picture are some of the non-determining parameters which are carried out. If the histopathologic reports show necrosis and detachment of the epidermis by an evident thickness (purely epidermal) it points towards SJS/ Toxic epidermal necrolysis.[12]

The first and foremost step in the management of SJS is the immediate withdrawal of the offending drug. The fluid and electrolyte imbalance should be appropriately maintained with the aid of sodium chloride and potassium chloride. The wounds often are self-healed as re-epithelization acts naturally. The drugs to be used in the management are not yet clear, but cyclosporine, corticosteroids, Tumor Necrosis Factor (TNF) inhibitors, thalidomide, high-dose intravenous immunoglobulins have been known to arrest the spread of the disease, if not, reduce the mortality risk.[12,13]

The severity of adverse drug reaction was evaluated by various causality assessment scales which include the following as Naranjo Scale[14], Alden Algorithm[15] and WHO-UMC scale.[16] The Naranjo Scale represented the event as "probable" whereas the WHO-UMC scaled marked the causality event as "likely/probable". Alden algorithm, specifically used to assess the drug casualty in SJS, marked the event at "probable".

CONCLUSION

With the easy availability of Nimesulide as an over the counter drug, adverse drugs reactions have aroused tremendously, wherein early identification and prompt discontinuation of the offending drugs are crucial for reducing clinical apparent infections and following complications of Stevens-Johnson Syndrome. Additionally, international countries such as Australia, US and Canada have banned the use of the drug whereas in India, it is subsequently being administered in adults. Henceforth, the safety profile should be monitored and all cases of adverse should be adequately reported.[18]

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