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Herbal medicine induced Steven Johnson Syndrome: A Case Report

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ABSTRACT

Steven Johnson syndrome is a severe and potentially lethal disease due to an immune-complex-mediated hypersensitivity reaction involving mucous membranes and skin. Steven Johnson syndrome and toxic epidermal necrolysis (TEN) are life-threatening diseases characterized by the detachment of skin and mucous membranes. It has been a common belief that herbal drugs do not cause such as much as side effects and toxicities as pure chemicals. Recently, SJS associated with herbal medicine has been reported. This paper aims to report a case of SJS marked with skin manifestations following the use of herbal drugs for the treatment of Alcohol withdrawal and Jaundice. A 28 years male old patient was admitted with complaints of Fever, Vomiting, and Rashes over the body. The patient had received herbal drugs for the treatment of Jaundice and Alcohol dependence. Herbal medicine still plays an important role in the Indian Healthcare system as it is one of the most ancient treatment systems in the Indian Healthcare system. Further studies may require to evaluate the characteristics of the general population and to identify any predisposing factors to SJS as recommended.

Keywords: Steven Johnson syndrome, Herbal drugs, Drug-induced reaction, Rashes, Skin lesion, Case report, adverse drug reaction, treatment, SJS, TEN.

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INTRODUCTION

Stevens-Johnson syndrome is a severe and potentially lethal disease due to an immune complex–mediated hypersensitivity reaction involving the mucous membranes and skin[1]. SJS occurs on a spectrum based on the total body surface area (TBSA) of the skin affected, with the most severe form referred to as toxic epidermal necrolysis (TEN), or Lyell's syndrome[1]. Their bullous mucocutaneous reactions (cutaneous and mucous membrane lesions including ocular, oral, and genital) are characterized by extensive necrosis and detachment of the epidermis[2]. SJS/TEN can lead to multi-organ to implicate which not only involved cutaneous and mucous membranes but also several internal organs[2]. Although it is difficult to diagnose early-stage SJS/TEN, biomarkers for diagnosis or severity prediction have not been well established. Furthermore, optimal therapeutic options for SJS/TEN are still controversial [3]. The increasing incidence of SJS/TEN with age is likely a result of more frequent drug prescriptions and co-morbidities that modify the drug effects[5]. Children show a high recurrence rate of SJS, 1 in 5 in the study by Finkelstein et al., suggesting vulnerability and potential genetic predisposition[5]. Oral manifestations of the disease, which are present in about 90% of cases, present as painful erythematous crusts and erosions with a greyish-white membrane[6]. Among nondrug-induced cases, Mycoplasma pneumonia infection has also been reported in association with SJS[6]. An association between onset of EM or SJS and intake of herbal drugs has been reported elsewhere as an extremely rare occurrence[7]

Classification of Stevens-Johnson syndrome:

1. Stevens-Johnson syndrome is known to be a "minor type of TEN" characterized by a detachment of less than 10% of the body surface area.
2. Overlapping Stevens-Johnson syndrome/toxic epidermal necrolysis: body surface area detachment of 10- 30%.
3. Toxic epidermal necrolysis: More than 30% of the body's surface area is detached[8].

The disease occurs in young adults usually men. The onset is sudden and runs 2-6 weeks with common recurrences almost occurring almost one to five times annually[9].

Among non-drug infectious causes, mycoplasma pneumonia in adults and herpes simplex virus infections in children are known to cause SJS/TEN[13]. A rare occurrence of TEN in a patient with severe aplastic anemia after allogeneic hematopoietic stem cell transplantation is also reported[13]. Lastly, vaccination is also implicated as inciting factors like human papillomavirus, mumps, measles, rubella, hepatitis B, influenza, anthrax, and tetanus vaccines[13].

TEN and SJS are considered a disease continuum, distinguished largely by their severity, as determined by the percentage of body surface area (BSA) affected by erosive blistering[12]. The

more severe presentation of TEN is always initiated by drugs, but the milder presentation of SJS can often be caused by infectious agents[12]. The mainstay of treatment is early identification and cessation of the culprit trigger and subsequent supportive care in a specialized burn intensive care unit(ICU) or similar high dependency unit[12].

TEN/SJS are rare, with reports ranging from two to seven cases per million per year[12].SJS, the less severe form, is three times more common in women than men, and people of all ages are affected[12]. Patients with malignancy, particularly hematological cancers and human immunodeficiency virus (HIV) are also at increased risk of SJS/TEN[12]. The mortality rate for TEN is 50% and 10% for SJS with a combined rate of 30%[12].Increased age and comorbidities are associated with greater mortality[12].

In this report, we describe a case of 28 years old male patient who has taken herbal treatment for Jaundice and Alcohol dependence which develops Steven Johnson Syndrome.

CASE REPORT:

A 28 years old male patient was admitted to Vijayanagar Institute of Medical Sciences (VIMS) in a male medical ward with complaints of Fever for 3 days, Vomiting for 3 days, Rashes for 3 days, and Generalized body ache for 2 days. The patient was a chronic alcoholic for 10 years. The patient does not have any past medical or past medication history. The patient does not have any family history related to the disease. The patient has received Ayurvedic drugs for the treatment of Jaundice and Alcohol dependence following which he developed rashes over his body, weakness, and fatigability. Examination revealed massive sloughing and hemorrhagic crusting of ulcers involving the buccal mucosa and mucocutaneous tissues in the perioral region. He was severely dehydrated and had a temperature of 107.5F. His body weight was 56Kgs. He explained that he was suffering from Jaundice for 15 days and had to withdraw alcohol and hence receive herbal drugs from a traditional healer (herbal medicine doctor, an Ayurvedic physician in India), who had prescribed him some solid jellies to be taken with milk and 10 Brown color tablets. After 1 hour of taking the drugs after he developed rashes throughout the body with vomiting and low-grade fever. After the occurrence of these symptoms, the patient went to a traditional healer. After seeing these symptoms the traditional healer advised applying another lotion over the body. As the symptoms worsen over time, the patient came to the hospital with his friends and was advised to be admitted to the hospital. On laboratory examination, his electrolytes were normal, Hb was 10gm%, Total count 12000, Neutrophils 64%, Lymphocytes 26%, and Eosinophils 5%.

He was given supportive therapy with IV fluids with Thiamine and protein supplements. Antibiotics were started to prevent secondary infection in the hospital. On Dermatology opinion

the patient was prescribed Liquid Paraffin, Cetrizne, and Corticosteroids. After further investigations and assays, a diagnosis of herbal drug-induced Stevens–Johnson syndrome was made. The patient fully recovered within 10 days.

Figure 1: Patient applied lotion to face and throughout the body

DISCUSSION

Stevens-Johnson syndrome is a severe and potentially lethal disease due to an immune complex–mediated hypersensitivity reaction involving the mucous membranes and skin[1.] SJS/TEN can occur in any individual but are more common in children and the elderly[1]. Although there have been cases reported after a viral illness (mainly herpes simplex) or mycoplasma infections, more than 90% of cases are medication-induced - the main culprits being antibiotics (sulphonamides and β-lactams), nonsteroidal anti-inflammatory drugs, and antiepileptics (phenytoin and carbamazepine)[1]. Although many mechanisms may involve in SJS/TEN, including reactive drug-mediated cytotoxicity, pharmacogenomics, infections, and so on, no convincing theory has appeared until now. Among them, most SJS/TEN are induced by drugs[2]. Although it is difficult to diagnose early-stage SJS/TEN, biomarkers for diagnosis or severity prediction have not been well established[3]. Furthermore, optimal therapeutic options for SJS/TEN are still controversial[3]. It has been a common belief that herbal drugs do not cause as many side effects and toxicities as pure chemicals[4]. How can this be defended when there are no reports of side effects of herbal drugs by herbalists and traditional medicine practitioners[4]? In India, many herbal drug practitioners (53·5%) prescribe allopathic drugs in the guise of an ethical cure[7]. Reports on allergic reactions to herbal

remedies exist in the medical literature[7]. The adverse effects of Traditional Medicine/Complementary Alternative Medicine (TM/CAM) are due either to the herbal product itself or added impurities (allopathic synthetic drugs), or a combination of both[7]. Traditional Ayurvedic and Chinese herbal medicines, which are often contaminated with arsenic and mercury may result in sensory loss and muscle wasting in addition to severe dermatological manifestations, such as Bowen's disease, and arsenical keratoses, reported elsewhere[7]. Stevens–Johnson syndrome has been reported following consumption of a healthy drink containing Ophiopogonis tuber[7]. Adverse drug reaction to herbal medicines can thus be a reaction to naturally- occurring medicinal plants, compounds, natural toxins, or to contaminants or adulterants in these

medicines. Treatment involves the withdrawal of culprit drug and supportive management which involves wound care, Fluid replacement therapy, nutrition, pain control and prevention; and treatment of infection[6]. This communication is a case report of Steven's Johnson Syndrome with which herbal drugs are associated.

Figure 2: Herbal drug-induced Stevens-Johnson Syndrome

CONCLUSION

Herbal medicine still plays an important role in the healthcare system in India. Because of its growing popularity, establishing a causal relationship in Herbal medicine-induced Steven Johnson Syndrome is an important task. Proper diagnosis and treatment of the disease are of major importance because mistreatment of the disease could be possible, due to variations of clinical manifestation. The ultimate goal of the management of this condition is the prevention of the development of secondary infection; reduce the risk of further trauma, and executive care for exudates and avoidance of softening of the skin. Apart from these, there are several

immunomodulating and immunosuppressive therapies have been proposed which includes corticosteroids, IVIG, cyclosporine, and TNF antagonist.

It is important to report and document serious adverse effects involving natural herbs and other treatment systems. It is also important that isolated chemicals from natural herbs undergo various clinical trials and toxicological trials before being widely used in drug therapy[4].Further studies in a larger sample size across India, comparing patient characteristics with the general population, to identify any other predisposing factors to SJS is recommended.

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