

An Illustrative Case Study on Drug Induced Steven-Johnson Syndrome by *Ginkgo biloba*

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Abstract

Steven Johnson syndrome (SJS) is a life-threatening illness usually associated with usage of medicines, which causes drug interactions. SJS seems to be one of the lethal drug reactions. Herbal medications are also responsible for these syndromes; many medications have been reported to cause SJS. Even though only few cases are described in the literature. It has important impact on the public health in view of its high morbidity and mortality. It is a severe hypersensitive reaction which belongs to type IV hypersensitive reaction. SJS are considered to resemble erythema multiforme with mucosal involvement. It mainly affects oral mucosal cavity. A drug named *Ginkgo biloba* was prescribed to the patient affected with vitiligo and also treated with allopathic medications for fever and headache. It caused an herbal drug interaction which eventually induced Steven-johnson syndrome. The patient has clinical manifestations such as fever, maculopapular rashes over anterior part of chest and ulceration all over mouth and lips. The patient was treated with rational antibiotic regimen and corticosteroids along with the withdrawal of herbal medications. Pharmacists have a vital role in evaluating a case study of patients and result superiority conclusion of the patient with an advice to withdrawal the medication and to monitor the interactions which was caused by the medications and their symptoms. This helps to improve the condition of the patient for better quality of life.

Keywords: Steven-Johnson syndrome, Hypersensitivity reaction, Oral mucosal cavity, Herbal drug interactions, Maculopapular rashes

Introduction

Stevens and Johnson is the one who described about this condition in 1922. Steven-Johnson syndrome may present as a general ailment leading to febrile, anonymous polymorphic lesions of the skin, a red skin rashes and ulceration on mouth, blisters on your skin and the mucous membranes of your mouth, nose, eyes and genitals, peeling of your skin within days after blisters form and mucous membrane characterized by acute blisters and erosions. Many cases which reported is drug- induced, affecting oral and peri-oral region. The incidence of SJS has been predicted to be around 1-6/1,000,000 persons per year with a mortality rate of 1-5% [1-3]. Steven-Johnson syndrome (SJS) is a rare, serious disorder of skin and mucocutaneous disorder which is severe form of erythema multiforme. It usually presents as erythematous macules evolving to epidermal detachment, vesicobullous lesions and mucous membrane erosions [4-6]. Steven-Johnson syndrome is a serious life-threatening skin condition and rare immune complex mediated hypersensitivity, which affects the skin and mucous membranes with huge mortality rate; since it can result as an immune response to an antigen or as drug reaction. Many causes of SJS are idiopathic. Drugs are considered to be one of the most common causes of Steven-Johnson syndrome. Siddha medicines are also known to cause this syndrome and many different categories of drugs have been reported [7-10]. It mainly occurs due to an adverse reaction to drugs which results in skin and mucosal eruptions that can be potentially fatal [11].

Case Report

A 13 years old male patient was admitted in male general ward of Thiruvallur government hospital with chief complaints of fever, maculopapular rashes over anterior part of chest and ulceration all over mouth and lips for a week. His dermatological examinations revealed that maculopapular rashes all over the chest started second day of fever followed by oral ulcer and white patches over the tongue. Patient has watery discharge from both of his eyes. The patient has the

complaint of difficulty in swallowing. On general examination; patient was conscious, febrile and lethargic at the time of admission. The patient has the history of vitiligo for which he was being treated with a siddha medication (*Ginkgo biloba*) since 1 month and he was treated with allopathic medicine for fever and headache by local medical practitioner. Figure 1a and 1b represents the condition for which the patient undergoes siddha medication.

The abdomen evaluation revealed that P/A was soft, and other observed parameters are normal. There was no evidence of any family history. No history of any triggers, trauma, infections, drugs and food allergy was reported by the patient. Patient condition was examined as mucosal ulceration over upper and lower lips. Ulceration present over entire right and left conical mucosa, tongue, palate and gingiva



Figure 1: (a and b) Patient undergoes siddha medication.

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of oral cavity. The siddha medications dispensed to patient for vitiligo are *Ginkgo biloba* and pungai oil (*Millettia pinnata*). The patient was advised to discontinue the siddha medication, and was treated with corticosteroids like Inj. Hydrocortisone 1 cc administered intravenously for first 2 days and Inj. Dexamethasone 0.5 cc administered intravenously for next 2 days, Syp. Paracetamol 10 ml given orally for a day behalf of fever, antibiotics are also suggested Inj. Taxim 1 g given intravenously twice a day for 2 days followed by 800 mg on last day and Inj. Amikacin 50 mg administered intravenously twice a day, additive therapy as Inj. Rantac to reduce GI effects in stomach, Tab. Cetirizine for allergic conditions in the skin, vitamin supplements such as Tab. Vitamin B complex and Tab. Vitamin C are also prescribed and tropical emollients like liquid paraffin was advised for application of rashes over the anterior part of chest for thrice a day and saline soaks over lips for thrice a day. The diagnosis of Steven-Johnson syndrome was made on the basis of clinical data and standard prescribing pattern (Table 1). Figures 2-4 represent the condition of a patient at time of admission.

The patient was observed and advised to withdrawal the siddha medications to improve the condition. The patient was on rational antibiotic regimen and corticosteroid along with regular counselling sessions, which included points regarding the disease, treatment and the lifestyle modifications. The patient was reviewed after a week. Rashes and Lesions had healed significantly in the oral cavity and on chest area. Figure 5a and 5b represents the condition of the patient after a week of therapy along with patient counselling illustrating marked improvement.

Discussion

Davydov et al. explains that *Ginkgo biloba* is a well-known drug, which was prescribed as a herbal medication to improve memory of a patient and the medication seems to has side effects with dermatitis. They also report an ADR of Stevens-Johnson syndrome due to the use of *Ginkgo biloba*. Patient was affected by two doses of *Ginkgo biloba* containing preparations which results in exfoliated rash, blistering and other symptoms consistent with SJS. Hence, they concluded that it is important for clinicians to be aware of this feasible side effect related to use of ginkgo preparations [12]. Metz et al. illustrates that their case reports an ADR of vasculitis rash induced by *Ginkgo biloba*. They also reported other adverse reactions, which is due to *Ginkgo biloba* include: increased risk of bleeding complications, dizziness and gastrointestinal upset [13]. Tomb et al. reported three cases of contact dermatitis due to female ginkgo tree [14]. Yuste et al. report the clinical manifestation of Stevens-Johnson syndrome in a 75-year-old male patient due to the ingestion of *Ginkgo biloba* [15,16].

With the aim of moving away from synthetic to organic world, patients are increasingly seeking herbal remedies to self-treat many diseases due to its safety profile. The use of siddha medications is economical in developing countries. Most adverse effects of drug-herbal interaction may involve in skin, liver, GI tract, renal toxicity and



Figure 2: Ulceration all over mouth and lips.



Figure 3: Maculopapular rashes all over the anterior chest area.

S.no	Diagnostic parameters	Units	Patient value	Normal value	Inference
1.	Temperature	°F	101°F	98.4°F	Increased
2.	Pulse rate (PR)	/min	104 beats	70-74	Increased
3.	Respiratory rate (RR)	/min	24 breaths	12-20 breaths	Increased
4.	Blood pressure (BP)	mm/Hg	110/70	120/80	Decreased
5.	White blood cells (WBC)	10 ⁹ /µl	7000	4000-11000	Within limits
6.	Red blood cells (RBC)	10 ⁹ /µl	4.31	3.8-4.8	Within limits
7.	Haematocrit (HCT)	%	31.3	41-59	Decreased
8.	Haemoglobin (HB)	g/dl	10.6	12-17	Decreased
9.	Mean corpuscular volume (MCV)	Fl	72.6	76-96	Decreased
10.	Mean cell haemoglobin (MCH)	Pg	24.6	27-32	Decreased
11.	Mean cell haemoglobin concentration (MCHC)	g/dl	33.9	31-35	Within limits
12.	Platelets (PLT)	10 ³ /µl	4.86	1.5-4.0	Increased
13.	Neutrophils	%	56.6	40-80	Within limits
14.	Lymphocytes	%	29.6	20-40	Within limits
15.	Monocytes	%	13.8	2-10	Increased
16.	Red blood sugar (RBS)	mg/dl	86	80-140	Within limits
17.	Serum creatinine	mg/dl	1.0	0.6-1.3	Within limits
18.	Urea	mmol/l	3.6	2.6-7.2	Within limits

Pg: Picograms, Fl: Femtolitres, µl: Microliters, dl: Decilitres, g: Grams, °F: Fahrenheit.

Table 1: Laboratorial parameters of patient.



Figure 4: Oral ulcer and white patches over the tongue.

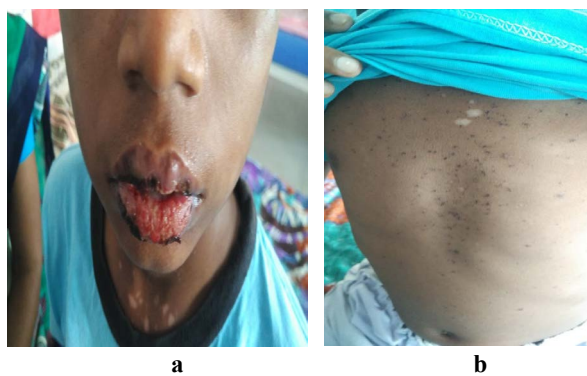


Figure 5: (a and b) Condition of a patient.

hepatotoxicity. There is often a misinterpretation that “natural” means “secure” and many patients trust that remedies of natural origin carry no risk and they don’t have known about siddha medication adverse effects with allopathic medications. However, siddha medications usually contain numerous constituents and it is not feasible to analyse them all. Adverse effects may also consequence from the erroneous use of wrong species of medicinal plants, inaccurate dosing, etc. The feasibility of errors in use of siddha medications can be due to both health care providers and customers. Through educational programs, awareness can be created on conventional drug-herbal interactions.

Conclusion

Steven-Johnson syndrome can be caused due to siddha medication such as *Ginkgo biloba*. SJS is usually caused by disorder of the immune system. The immune reaction can be triggered by infections, drugs or medications. Diagnosis and proper treatment of the ailment is of a high significance because improper treatment of the patient could be feasible, due to the difference of clinical manifestations. Now days, siddha medication consumption has increased while the safety of medications remains under examined. In this case, the intake of siddha medications was interacted with allopathic medicines. These severe adverse effects were caused by siddha drugs and patients use as self-medication may cause difficulties in diagnosis and management. Additionally, the patient was instructed about the adverse effects and advised to taper the use of over the counter medications and any other ayurvedic or siddha medications which can aggravate the present

condition. Pharmacists have a vital role in evaluating a case study of patients and result superiority conclusion of the patient with an advice to withdrawal the medication and to monitor the interactions which was caused by the medications and their symptoms. This helps to improve the condition of the patient for better quality of life.

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Compliance with Ethical Standards

Written informed consent was obtained from the patient for publication of the case study, inclusion of the accompanying images. Copies of written consent may be requested for review from the corresponding author.

Conflict of Interest

The authors declare no conflicts of interest concerning the content of this case report.

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