



### Case Report

## TRIBULUS TERRESTRIS-HERBAL DRUG INDUCED STEVEN JOHNSON SYNDROME: A CASE REPORT

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### ABSTRACT

*Tribulus terrestris* is an ayurvedic medication which is traditionally used because of its aphrodisiac and antiurolithiatic activities with complete inhibition of stone formation. Steven-Johnson syndrome is a cytotoxic immune reaction to drugs and infections. This is a case report of *Tribulus terrestris* induced Steven-Johnson syndrome in geriatric women.

**KEYWORDS:** *Tribulus terrestris*, Steven-Johnson syndrome, Adverse drug reaction.

### INTRODUCTION

Stevens-Johnson syndrome (SJS) is a life-threatening skin reaction characterized by extensive epidermal detachment [1]. SJS is rare with incidence of 0.05 to 2 persons. A global population-based study had previously reported that the incidence of SJS and TEN is estimated 1.0 to 6.0 per million and 0.4 to 1.2 per million [2]. Complications of SJS and TEN include microalbuminuria and presence of renal tubular enzymes in urine, use of previous herbal medicines, arthralgia, hepatitis, encephalopathy, Kidney injury and myocarditis [3]. TEN can be induced by drugs or infection or can be idiopathic. Medications are the major precipitating factors. Some of the ayurvedic drugs like *Tribulus terrestris* have a worldwide distribution. Its roots, seeds, fruits, and leaves had been traditionally used for therapeutic purposes in particular urolithiasis [4]. *Tribulus terrestris* is a flowered herb that grows in many parts of the world. These herbs commonly used in many of the diseases like hypertension, diabetes, and nephrolithiasis leads to adverse effects [5]. The adverse drug reaction is due to type-4 hypersensitivity reaction which is recognized as a dysregulation of cellular immunity [6], caused by a release of various cytotoxic signals including granulysin. SJS may present as nonspecific febrile illness (malaise, headache, cough, rhinorrhea) with polymorphic lesions of skin and mucous membrane characterized by acute blisters and erosions [7]. The pathophysiological mechanism is not fully understood. It is due to delayed hypersensitivity reaction mediated by T-cells. Some

individuals have a genetic predisposition to develop such disorders: the acetylators, deficient in enzymes involved in the destruction of toxic drug metabolites, such as glutathione transferase. Recently, genetic association of some HLA major histocompatibility complex alleles with the occurrence of serious drug reactions has been described [8]. Complete blood count (CBC) may show an unspecific leukocytosis or even indicate secondary bacterial infection. Cultures of blood, urine and skin may reveal the agent of the underlying suspected infection [9]. Skin biopsy is the final examination and reveals necrosis in all layers of the epidermis caused by apoptosis of keratinocytes and epidermal detachment, while the dermis shows minimum inflammatory changes. In SJS and TEN, greater results were obtained by supportive care alone compared to administration of Glucocorticoids or Intravenous immunoglobulin (IVIG), in reducing the associated mortality. Early referral to the intensive care unit is required. They may refuse to clear due to pain resulting from urethritis or balanitis or vulvovaginitis which requires catheterization. Feeding by nasogastric tube is often required. Careful adherence to oral hygiene is needed to avoid more infection [10]. Corticosteroids have a controversial role in the treatment of SJS. Cyclophosphamide and cyclosporine have been used with less success. One clinical trial has shown the successful treatment of TEN with IV immunoglobulin's [11].

### CASE STUDY

A 55-year-old woman was admitted in hospital with an erythematous skin rash involving bullous throughout the body and oropharyngeal ulceration developed within five days after consumption of herbal medicine (*Tribulus Terrestris*) to treat renal calculi. The patient had a history of right renal calculi and AKI. On examination, the patient was mild pallor and ill. Her body temp was 99.6°F, BP was 110/70 mmHg, PR was 88/minute and RR was 20/minute. Tenderness is evident when the skin is affected with rash and Nikolsky's sign was positive. The WBC was 3.2/mm<sup>3</sup>, platelet count was 132,000/mm<sup>3</sup>, PCV was 26.2 volume %, MCV was 69.9 fl, MCH was 22.2 pg/cell and MCHC was 3g/dl. Her C-reactive protein

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(CRP) was raised to 15.6mg/dL. The levels of total protein were 5.6g/dL, albumin was 3.2ng/mL, serum urea was 89mg/dL and serum creatinine was 2.5mg/dL. "After" the diagnosis of TEN with sepsis patient was treated with Intravenous administration of immunoglobulin- G (IVIG) at 1g/kg/day for 3 days. Intravenous fluids for thermoregulation and Intravenous Dexamethasone 8mg for thrice daily to treat blisters, injection Metronidazole 500mg thrice daily to treat sepsis, Clonate-F cream was used for skin infections, for oropharangeal ulceration candid mouth paint 10ml thrice daily and High protein diet was suggested. The treatment was continued for 4 days and on day-5 the patient situation was aggravated and admitted in ICU and treated with Intravenous immunoglobulin- g 5gm slowed infusion for 3 hrs, Injection Avil 2cc and intravenous hydrocortisone 100mg. After 1-hour patient vitals were low and treated with injection Adrenaline 1<sup>st</sup> dose, 2<sup>nd</sup> dose and 3<sup>rd</sup> dose but the code BLUE announced because the patient is unresponsive, pulse is non-palpable and BP is not recordable. CPR was done and continued with defibrillators but the patient was still unresponsive. "Finally" by ECG shows a flat line and her pupils were B/L fixed dilated and declared as dead.

### DISCUSSION

In this modern age, majority of the people are affected by UTI and Kidney stones owing to unhealthy food habits. Indigenous systems like ayurvedic and unani remedies have lot of literature and prescriptions related to the calculi. In this case the patient has taken Tribulus terrestris since it is believed and used in folk medicine for tonic, aphrodisiac, palliative, astringent, stomachic, antihypertensive, diuretic, lithotropic and UTI agents [12] and as a result she has been presented with skin inflammation i.e., blisters and itching all over the body along with oropharangeal ulcers which is termed and diagnosed as Steven-Johnson syndrome. This herbal drug induced Steven Johnson syndrome and acute kidney disease share a similar mechanism involving T-cells. These pathways include excessive infiltration of inflammatory cells, such as macrophages, lymphocytes, eosinophils, and mast cells, infiltrating skin lesions, as well as a high level of serum IgE [13]. Patient was suggested to cease the causative agent - Tribulus terrestris since early withdrawal of the offending agent will improve the overall prognosis and was prescribed with the hydration therapy along with Dexamethasone and Immunoglobulin's with other supportive care. As a primary treatment, supportive measures including special attention to the airways, preventing secondary infection, pain control, maintenance of venous access distance from the affected area [14,15] were given to the patient, but the patient couldn't able to sustain the symptoms or toxicity that leads to the death.

In a previous study, a seven year old boy has been presented with SJS symptoms were managed by the same hydration as well as nutritional support along with Immunoglobulin's. In another survey, 28 year old man admitted with two episodes of seizures, followed by weakness in lower limbs, malaise and poor appetite. Investigations revealed that he has been taken Tribulus terrestris which diminished his kidney function. After the withdrawal, his kidney as well liver functions improved spontaneously along with supportive care [16]. Due to the long term use of the herbal drug Tribulus terrestris, we are unable to anticipate the good prognosis of our patient. This herbal drug has elicited severe toxicity and aggravated the patient condition that progressed to end-stage and proved as fatal.

### CONCLUSION

The mortality of the present study was higher than in previous studies, which may stem from the fact that use of Tribulus terrestris played a major role in people who are using this for kidney stones. Hence our result suggests the necessity of improving the knowledge about various herbal medications and their benefits vs risk ratio than the other prescribed treatment by the physicians. This case study suggests that avoid the herbal medications particularly to the people who are living in remote areas since many studies revealed the use of them to be fatal and can cause death.

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