

# A Case of Stevens-Johnson Syndrome Probably Induced by Herbal Medicine

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#### Dear Editor:

Stevens-Johnson syndrome (SJS) is a life-threatening skin reaction characterized by extensive epidermal detachment<sup>1</sup>. Drugs, especially sulfa drugs, anti-epileptics, and antibiotics, are the most common causes<sup>1</sup>, but recently, SJS associated with herbal medication has been reported<sup>2</sup>. Herein, we report a case of SJS probably induced by herbal medicine. We received the patient's consent form about publishing all photographic materials. The study protocol was approved by the Institutional Review Board of Incheon St. Mary's Hospital, The Catholic University of Korea (IRB no. OC17ZESI0049).

A 77-year-old man presented with a sudden onset of bullous lesions on his trunk and extremities (Fig. 1). The histopathological findings were sub-epidermal split with extensive epidermal necrosis (Fig. 2). The direct immunofluorescence findings were negative. Days after the skin biopsy, the vesicles and bullae began to fuse, rapidly progressing into skin erosion and denudation. The mucous membranes of the mouth and conjunctiva were also affected. Epidermal detachment was seen in less than 10% of the body surface area and the Nikolsky sign was present. The patient answered that there has been no change in his routine medication for the past 3 years, but mentioned that he started on herbal medication a month ago. The herbal medication was said to contain deer antlers, ginseng, camphor etc. Based on severity-of-illness score for toxic epidermal necrolysis, our patient's ex-



Fig. 1. Multiple erythematous tense bullae on the buttock and both extremities.

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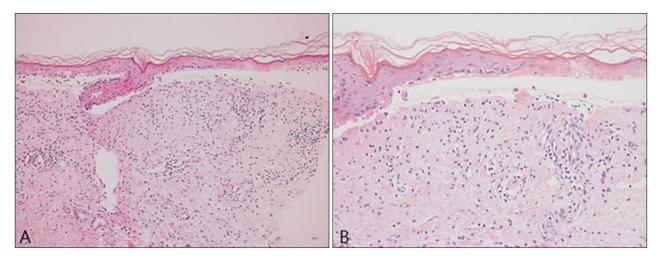


Fig. 2. (A) Biopsy specimens from the arm revealed a subepidermal split with bullae and epidermal necrosis (H&E,  $\times$ 100). (B) (H&E,  $\times$ 200).

pected mortality rate was 12.1%. He was asked to immediately stop the herbal medication. The patient made a full recovery after a course of intravenous steroid therapy, daily dressings and supportive care.

According to prior reports, the patch test results varied among SJS patients with culprit drug. Lin et al.<sup>3</sup> reported that while 62.5% of patients with carbamazepine-induced SJS/toxic epidermal necrolysis (TEN) show positive patch test results, patch tests for allopurinol-induced SJS/TEN are mostly negative. As for our case, we were not able to perform a patch test on herbal medicine because the patient refused.

Differential diagnoses of SJS include exfoliative dermatitis, staphylococcal scalded skin syndrome (4S), bullous pemphigoid (BP), paraneoplastic pemphigus and bullous erythema multiforme (EM). Although exfoliative dermatitis resembles SJS clinically, it rarely affects the mucosa. There is an intra-epidermal separation in 4S unlike SIS, which shows a sub-epidermal split. BP usually shows a gradual onset and spares the mucosal area. Paraneoplastic pemphigus is usually associated with an underlying cancer. As for our patient, the cancer screening tests were negative. Bullous EM is commonly triggered by herpes simplex virus infection and presents with characteristic targetoid lesions. More than 100 drugs have been reported as potential cause of SJS<sup>4</sup>, but herbal medicine induced SJS has not yet been reported in the Korean literature. Recently, several studies have reported the relationship between the human leukocyte antigen (HLA) genotype and drug hypersensitivity. Although the HLA genotype of the herbal induced SJS remained uncertain. Herbal medications carry a mixture of ingredients that originate from plants and animals. Because of this characteristic, identifying the culprit ingredient within the herbal medication is extremely difficult. Also, since there is no obligation to notify the ingredient within the medication packet, scientific evaluation in case of adverse events are nearly impossible. Herbal medication induced drug eruption can be caused by herbal medicine itself, but also by added impurities and the combination of ingredients<sup>5</sup>. With the lack of patch testing and being unable to identify the full ingredient of the herbal medicine, the authors were not able to confirm that our SJS is caused by herbal medicine. However with the clinical circumstances, we believe that herbal medicine is most likely the culprit drug in our case. We report this case because we think it is important that dermatologists consider the possibility of herbal medicine-induced drug eruption and notify the public about the potential serious side effects of herbal medicine.

### CONFLICT OF INTEREST

The authors have nothing to disclose.

## **REFERENCES**

- 1. Gerull R, Nelle M, Schaible T. Toxic epidermal necrolysis and Stevens-Johnson syndrome: a review. Crit Care Med 2011;39:1521-1532.
- Bonhomme A, Poreaux C, Jouen F, Schmutz JL, Gillet P, Barbaud A. Bullous drug eruption to Nigella sativa oil: Consideration of the use of a herbal medicine - clinical report and review of the literature. J Eur Acad Dermatol Venereol 2017;31:e217-e219.
- 3. Lin YT, Chang YC, Hui RC, Yang CH, Ho HC, Hung SI, et al. A patch testing and cross-sensitivity study of carbama-

- zepine-induced severe cutaneous adverse drug reactions. J Eur Acad Dermatol Venereol 2013;27:356-364.
- 4. Yoon J, Oh CW, Kim CY. Stevens-johnson syndrome induced by vandetanib. Ann Dermatol 2011;23(Suppl 3):
- S343-S345.
- 5. Lim YL, Thirumoorthy T. Serious cutaneous adverse reactions to traditional Chinese medicines. Singapore Med J 2005;46:714-717.

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# Schnitzler Syndrome: A Case Report and Review of Literature

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#### Dear Editor:

Schnitzler syndrome (SchS) is a rare autoinflammatory disease characterized by a recurrent urticaria and monoclonal gammopathy<sup>1</sup>. Herein, to our knowledge, we report the first case of SchS in Korea. The study protocol was approved by the Institutional Review Board of Seoul St. Mary's Hospital, The Catholic University of Korea (KC16ZISE0262).

A 64-year-old man presented with two year history of daily urticaria. On physical examination, wheals and erythematous patches were found on the trunk and both extremities (Fig. 1). In contrast to most patients with urticaria, there was no pruritus, and antihistamine therapies did not have any effect. Only systemic steroid treatment yielded transient symptom improvement. The individual lesions lasted about 24 hours and resolved completely.

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Associated symptoms were musculoskeletal pain, and bouts of fever. Laboratory investigations showed leukocytosis (10.57×10<sup>9</sup>/L), an elevated erythrocyte sedimentation rate (77 mm/hr; 0~20 mm/hr) and an increased C-reactive protein (CRP) level (11.95 mg/L;  $0.01 \sim 0.47$  mg/L). Increased immunoglobulin (Ig)M levels (852 mg/dL; 46~ 260 mg/dL), decreased IgG (831 mg/dL; 870~1,700 mg/dL) and IgA (99 mg/dL; 110~410 mg/dL) were detected. Elevated levels of free kappa light chain (32.95



Fig. 1. On physical examination, wheals and erythematous patches were found on the trunk and both extremities.