Received: 10 Sep 2023 | Revised: 20 Oct 2023 | Accepted 22 Oct 2023

doi.org/10.61853/cds.14750

Clinical Dermatology and Surgery

Idiopathic UV-Induced Steven Johnson Syndrome: A Case Report

Michelle Zydeck[1], Amritpal Kooner, MA[1]; Conor Dolehide, MD[1]

1. Chicago College of Osteopathic Medicine, Midwestern University, Downers Grove, IL, 60515

Corresponding Author
Michelle Zydeck
Chicago College of Osteopathic Medicine
555 31st St
Downers Grove, IL 60515
United States
Phone: 1 734-718-8303
Email: michelle.zydeck@midwestern.edu

ABSTRACT

Stevens-Johnson syndrome (SJS) is considered a life-threatening adverse drug reaction associated with high mortality. This condition can be influenced by many factors such as pharmacokinetics, pharmacodynamics, immune response and infective agents. Anticonvulsants and antibiotics are among the drugs that were predominantly suspected of triggering SJS. There are currently no standardized treatment guidelines for SJS. The usual treatment is the withdrawal of the suspected causative agent and supportive therapy.[3] We report a case of a 31 year old male who presented to the emergency room with a full body rash and sores in the mouth and groin. The patient exhibited erythema in his eyes, suggesting ocular involvement. In addition, the lips and oropharynx revealed heme crusting and erosions. The patient was not currently on any medication. Previous cases have shown SJS as a result of medication or infections, however the manifestation of SJS after prolonged sun exposure is unique to the literature. This case provides valuable insights into idiopathic uv-induced SJS and the impact/importance of rapid treatment on various forms of SJS.

BACKGROUND

Stevens-Johnson syndrome (SJS) is a rare, life-threatening disease that is characterized by extensive epidermal detachment, erosion of mucous membranes and severe systemic symptoms. In the majority of cases, the development of symptoms can be attributed to a severe type 4 hypersensitivity adverse reaction to drugs, most commonly antibiotics. TEN and SJS symptoms result from massive apoptosis of epithelial cells, and are considered to be two ends of a spectrum of severe epidermolytic adverse cutaneous drug reactions, differing only by their extent of skin detachment. If epidermal detachment

is <10% it is considered Steven Johnson Syndrome.[1]

The beginning stages of SJS resemble those of the flu, with a temperature, sore throat and fatigue. Within 1-3 days of this, the mucous membranes in the genitals and the eye sockets become inflamed and ulcers or blisters begin to form. Skin lesions will have variable severity and can change into vesicles, bullae or detachable skin necrosis. Erythema is the main cutaneous finding, however the Nikolsky sign can aid in diagnosis and is defined as an epidermal detachment caused by the application of pressure on skin.[3] Multiple organ systems, such as cardiovascular, pulmonary, gastrointestinal, and urinary systems can also be affected. The most common complication reported in SJS patients is secondary bacterial skin infection.[3]

Anticonvulsants, antibiotics and non-steroidal anti-inflammatory drugs (NSAIDs) are the more common triggers. In order to consider SJS as drug related, the affected patients must be exposed to the suspected drug within 8 weeks prior to the occurrence of the rash.[3]

Diagnosis relies mainly on clinical signs together with the histological analysis of a skin biopsy showing typical full-thickness epidermal necrolysis due to extensive keratinocyte apoptosis.[2]

CASE PRESENTATION

A 31 year old male presented to the emergency room (ER) with a rash that had developed over the course of four days. The patient reported experiencing full body rash, including palms, along with sores in the mouth and groin. Other pertinent history included a fever of 101 degrees Fahrenheit, sore throat, and body aches four days prior to presentation. Strep test was negative and patient was suspected for mononucleosis due to presence of a nutmeg rash. Upon examination, the patient exhibited erythema in his eyes, suggesting ocular involvement. Examination of the lips and oropharynx revealed heme crusting and erosions.

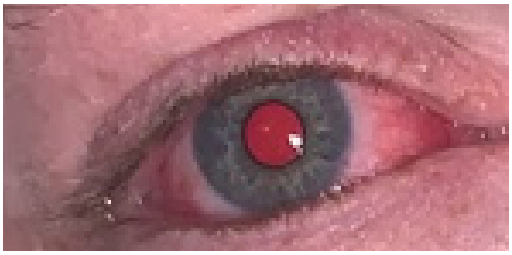

Figure 1: *Conjunctival erythema and inflammation of surrounding tissues*

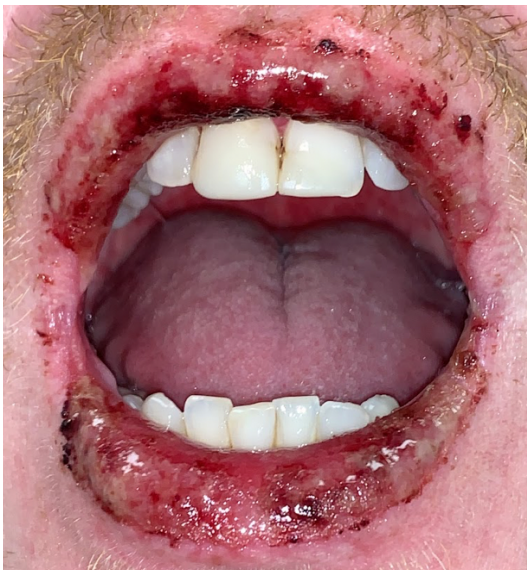

Figure 2: *Well-defined perioral erosions of mucosal and cutaneous epithelial loss and ulceration*

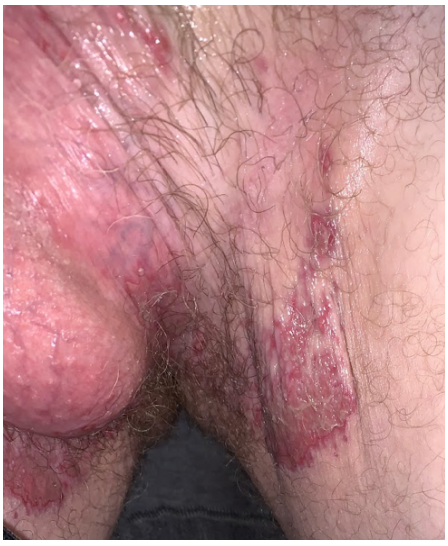

Figure 3: *Diffuse, intense, and inflammatory redness in inguinal region*

The patient's neck was supple and his trunk displayed central scattered erythema, with photodistributed erythema on his neck and head. Furthermore, erythema was noted in his groin and scrotum.

At this time the patient was prescribed Benadryl, eye drops, and oral prednisone & azithromycin for 2 days.

DISCUSSION

Drug-induced SJS/TEN may be caused by dysregulation of cellular immunity. Cytotoxic T lymphocytes and natural killer cells may recognize offending drugs or their metabolites presented by human leukocyte antigen (HLA) class I molecules on keratinocytes. When these immune cells are activated, various cytotoxic signals, including Fas/Fas ligand, perforin/granzyme B and granulysin are released to mediate keratinocyte apoptosis and detachment of skin and mucous membranes.[3]

T lymphocytes, particularly CD8+ lymphocytes, are present in a large amount in blister fluids Moreover, skin lesions, blister fluids/cells, peripheral blood mononuclear cells, or plasma of patients with SJS contained an increased number of cytokines that are responsible for proliferation and activation of T cells. They include IFN-g, IL-2, IL-5, IL-6, IL-10, and IL-13. In addition, tumor necrosis factor-alpha (TNF-alpha) is released by keratinocytes and macrophages in plasma and blister fluids and it may also contribute to keratinocyte apoptosis.[3]

The management of SJS requires immediate discontinuation of the causative drug and the start of supportive care. This includes monitoring of fluid balance and electrolytes, respiratory and nutritional support. Pain management can provide patient relief and include the administration of analgesics and topical anesthetics. Wound treatment can reduce the complications that result from the loss of the skin barrier and includes debridement of broken blisters, removal of necrotic skin, topical antiseptics or antibiotics, bandages and a warm environment.[5]

Certain adverse drug reactions are strongly associated with variation in the HLA genes. Examples include the HLA-B*15:02 allele and carbamazepine-associated SJS and the HLA-B*58:01 allele and allopurinol-associated SJS.[6] However, only a small percentage of the population (<10%) with an HLA risk allele will develop SJS after exposure to the culprit drugs.

Randomized controlled studies for the treatment of SJS/TEN are lacking as it is a rare condition, and is associated with a high rate of mortality. There is a therapeutic role of intravenous immunoglobulin (IVIG) which is related to the direct inhibition of FAS/FAS ligand interaction.[5] Many studies showed that patients treated with high dose IVIG in the first 4 days after the beginning of skin lesions had a better recovery and a higher survival rate.[3] The therapeutic role of corticosteroids has also been evaluated. Some studies found that high doses of dexamethasone were effective, especially when they are used at the beginning of the disease. However there is a higher risk of complications, such as gastrointestinal hemorrhage and sepsis with corticosteroid use.[3] Overall the timing for corticosteroid systemic administration, the corticosteroid type, dose and the treatment duration are still not clearly defined.

A meta analysis did not find any difference between corticosteroid, IVIG and supportive care in reducing mortality.[4] The analyzed series comprised a total of 439 patients. Supportive care was used in 199 patients ($p = 0.43$), corticosteroids were administered to 78 patients ($p = 0.84$) and

IVIG in 162 ($p = 0.23$).[4] In recent years it has become widely suggested to administer IVIG at high dose (2-4 g/kg) for 4 days followed by corticosteroids.[3]

Recent studies have also discussed the use of immunosuppressive treatment with TNF-α inhibitors. Infliximab and etanercept have shown to be effective at halting disease progression.[7]

CONCLUSION

The identification of new clinical presentations for SJS is important for early diagnosis and treatment to reduce mortality. UV induced SJS without the presence of medication or infection shows another way SJS can present. The advancement of current literature on presentation, immunopathogenesis, and treatment guidelines serves as a valuable resource for future research endeavors and reinforces the need for ongoing research to reduce mortality and lessen treatment time.

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