Received: 2018.07.16
Accepted: 2018.09.19
Published: 2018.12.21

e-ISSN 1941-5923
© Am J Case Rep, 2018; 19: 1519-1521
DOI: 10.12659/AJCR.912123

Stevens Johnson Syndrome with Vaginal Pain and Lesions as Initial Presentation

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

EF 1 **Reid Mergler**
ABEF 2 **Meleen Chuang**

1 Albert Einstein College of Medicine, Bronx, NY, U.S.A.
2 Department of Obstetrics Gynecology and Women's Health, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY, U.S.A.

Corresponding Author: Meleen Chuang, e-mail: Mechuang@Montefiore.org
Conflict of interest: None declared

Patient: Female, 27
Final Diagnosis: Stevens Johnsons syndrome
Symptoms: Vaginal ulceration
Medication: TMP-STX
Clinical Procedure: —
Specialty: Dermatology

Objective: Unusual clinical course
Background: Stevens Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are causes of rare but life-threatening emergencies characterized by desquamation of the skin and mucosa. As SJS most commonly presents with skin rash followed by mucosal involvement, we present a case of vulvovaginal lesions as the initial presentation with progression to SJS after re-exposure to the culprit drug.
Case Report: A 27-year-old female with acute cystitis was given trimethoprim-sulfamethoxazole. After 2 days, she reported vaginal pain. Three days later, she was hospitalized with vulvovaginal ulcerations and restarted on trimethoprim-sulfamethoxazole, leading to worsening vaginal lesions with rapid desquamation of conjunctival and oropharyngeal involvement. Biopsies of arm lesions revealed SJS.
Conclusions: It is important to recognize SJS as a rare but life-threatening cause of vulvovaginal ulceration, as early diagnosis is vital for successful treatment.

MeSH Keywords: Female Urogenital Diseases • Stevens-Johnson Syndrome • Trimethoprim-Sulfamethoxazole Combination

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/912123>

1343 — 1 8

Background

Stevens Johnson syndrome (SJS) is a rare but life-threatening cause of a cutaneous drug reaction characterized by extensive epidermal detachment, mucosal erosion, and constitutional symptoms. The classic presentation of SJS with toxic epidermal necrolysis (TEN) usually starts with flu-like symptoms including fever and upper respiratory tract symptoms with subsequent development of a maculo-papular skin rash followed by detachment of 2 separate mucous membranes (oropharyngeal, conjunctival, anogenital, and nasal membranes) [1].

Several reviews report that antibiotics, anticonvulsants, and non-steroidal anti-inflammatory drugs are the most common medications responsible for SJS/TEN [2]. Trimethoprim-sulfamethoxazole (TMP-SMX) is thought to be one of the main drugs associated with SJS/TEN. Several studies have reported up to 20% of SJS cases involved exposure to this drug. The study by Guillaume et al. evaluated 87 patients with TEN in their dermatological intensive care unit, and the culprit drug was determined in 67 patients (77%). In their study, the mean time from first drug administration to onset of TEN was 13.6 ± 8.4 days [2]. Often, the offending agents have already been removed at the time of hospital admission when the diagnosis is made, but not at the onset of the symptoms.

We present a case of SJS that is interesting in several respects. The patient had never taken TMP-SMX prior to her initial exposure and had only vaginal lesion and pain without any constitutional symptoms or mucosal involvement. Four days later, the patient had re-exposure to the offending agent that led to further progression of SJS, with rapid worsening of vaginal lesions and immediate progression to more commonly seen presentation of involvement of the oropharynx and the conjunctiva with desquamation of skin and acute decompensation within 2 days. The documented second exposure of the culprit drug, along with the immediate worsening of the patient's clinical symptoms within 12 hours of taking the second dose has rarely been described in the literature.

Case Report

A 27-year-old female P0 with a history of polycystic ovary syndrome (PCOS) was seen in the clinical office with complaints of dysuria; she was diagnosed with urinary tract infection and prescribed TMP-SMX. After taking 4 doses of TMP-SMX, the patient called the office noting left labial swelling and pain and presented to the emergency department (ED). In the ED, she was evaluated and diagnosed with left vulvovaginitis and discharged home after various cultures were obtained. She discontinued TMP-SMX after negative urine cultures. The patient returned to the ED 2 days later with worsening vulvar

lesions and more vaginal pain. The cultures initially obtained were all negative (herpes simplex, chlamydia/gonorrhea, and wound cultures). She was discharged home with sitz bath and supportive care; she was advised to follow-up in the clinic office. Seven days following her initial dose of TMP-SMX, she presented again to the clinic and was admitted for workup of vulvar cellulitis. On initial hospitalization, she was afebrile, had vulvar pain and the vaginal lesions turned into an ulcer, however, she had no other complaints. She was evaluated and started on TMP-SMX for concerns of vulvar cellulitis with possible underlying abscess.

After she received 2 doses of TMP-SMX, the patient had new lip swelling, periorbital swelling, facial swelling, and formation of thick white plaque on her tongue and mouth. She also developed an erythematous papular pruritic rash on her hands, arms, soles of the feet bilaterally and papules noted on the legs (up to thighs), feet, and abdomen. There were also areas of early vesicle formation and some skin sloughing. On genital examination, she had significant erythema and edema over the bilateral labia with shallow ulcerations. The patient also had new onset fevers and was febrile to 37.8°C (102°F). The patient was otherwise healthy, without medical or surgical history, and no history of drug allergies. The patient remained febrile with new onset sore throat and difficulty swallowing that required immediate otolaryngology (ENT) evaluation. Flexible laryngoscopy by ENT showed white plaques on her tongue with areas of desquamation of the oral cavity mucosae with some white exudates.

The patient reported swelling of her eyes, and a new-onset painful maculopapular skin rash. Dermatology was consulted and the diagnosis of SJS was made. Dermatology consult biopsied a skin lesions and the patient was transferred to the burn unit/ICU for immediate supportive care.

The pathology (shown in Figure 1) showed classic histopathological findings of interface dermatitis with many necrotic keratinocytes, in which the diagnosis of SJS was made. The patient had a self-limited course of SJS, and she was treated successfully with intravenous immunoglobulin (IVIG), supportive care, and wound care. She was discharged home 11 days after her hospital admission with resolution of all lesions.

Discussion

In this case report we briefly review TEN and SJS as well as describe the unique presentation of vulvovaginal lesions as initial mucosal involvement. In our patient's case, the only presenting symptom was vulvovaginal swelling and vulvar ulceration, which has not previously been reported in the literature. One case report in the literature detailed the use of

Figure 1. A punch biopsy of skin from this patient demonstrated full thickness epidermal necrosis with minimal dermal inflammation (20× photo) (Courtesy of Dr. Agean Chan).

terconazole vaginal suppository associated with fatal TEN [4], but that case did not have vulvar lesions as the first presenting symptom of SJS.

SJS/TEN most typically presents 8–12 days after drug exposure with fevers, flu-like symptoms, respiratory involvement followed by macular papular lesions and desquamation of affected areas including oral, nasopharyngeal, conjunctival, and anogenital involvement [3]. Eventually, as the lesions progress, it involves the full thickness of the skin with necrosis and exfoliation of the epidermis. After the initial skin lesions form, mucosal involvement on the mouth, eyes, and the vagina is characteristic [3–5].

Our patient did not have any prior risk factors or prior drug exposures besides the TMP-SMX, she was not on metformin or any medications for her PCOS, and a literature review search did not find any direct association between PCOS and increased risk for SJS.

Overall, there are more than 2 hundred medications commonly associated with SJS/TEN including antibiotics, anticonvulsants, non-steroidal anti-inflammatory drugs, allopurinol, and corticosteroids. Drug-induced SJS/TEN accounts for 80–95% of cases,

and among these medications, sulfonamides have the highest association with TEN accounting for up to 30% of the drug-induced cases [6]. The exposure of TMP-SMX twice is noted in the literature, where up to 19% of patients with SJS/TEN had manifestation of disease only after a second exposure to the medication in their lifetime [2]. It is not known how these medications cause TEN, but some research suggests an association with immunological processes involving cytotoxic T cells and natural killer cells [7].

Conclusions

Our case has several unique features. SJS usually occurs after between 7 days to 2 months of drug exposure with a mean time of onset ranging from 6 days to 2 weeks [8]. Our patient had worsening symptoms and developed SJS after a second dose of oral antibiotic within 6–12 hours. Several studies support this finding as they have demonstrated that SJS/TEN may occur within a few hours on re-exposure to the causative drug [6–8]. Another distinct aspect of our case was the initial presentation. The patient had vaginal pain for 3 days after exposure to TMP-SMX with subsequent vaginal mucocutaneous desquamation. This differs from the usual prodromal flu-like symptoms followed by maculopapular skin desquamation. Even severe skin manifestation in the absence of prodromal symptoms is extremely rare and has been mentioned in only a handful of published cases. Since vulvovaginal swelling and lesion were the sole complaints, it was difficult to consider SJS/TEN as a differential diagnosis.

Because the patient was exposed to the causative medication in the hospital, we were able to follow the natural progression of her symptoms. As soon as the prodromal symptoms, fevers, and skin findings erupted, there was acute decompensation within 12 hours of TMP-SMX re-exposure. Since we identified the causative drug, made the diagnosis, discontinued the medication and started IVIG and supportive care, the patient was able to make a full recovery with resolution of most of her symptoms. This report shows that although SJS is a rare diagnosis, provider should consider SJS as a possible differential diagnosis as a cause of vaginal lesion after exposure to drugs.

References:

- Gerull R, Nelle M, Schaible T: Toxic epidermal necrolysis and Stevens-Johnson syndrome: A review. *Crit Care Med*, 2011; 39: 1521–32
- Guillaume JC, Roujeau JC, Revuz J et al: The culprit drugs in 87 cases of toxic epidermal necrolysis (Lyell's syndrome). *Arch Dermatol*, 1987; 123: 1166–70
- Bastuji-Garin S, Rzany B, Stern RS et al: Clinical classification of cases of toxic epidermal necrolysis, Stevens-Johnson syndrome, and erythema multiforme. *Arch Dermatol*, 1993; 129: 92–96
- Searles GE, Tredget EE, Lin AN: Fatal toxic epidermal necrolysis associated with use of terconazole vaginal suppository. *J Cutan Med Surg*, 1998; 3: 85–87
- Gupta LK, Martin AM, Agarwal N et al: Guidelines for the management of Stevens Johnson syndrome/toxic epidermal necrolysis: An Indian Perspective. *Indian J Dermatol Venereol Leprol*, 2016; 82: 603–25
- Wolkenstein PE, Roujeau JC, Revuz J: Drug-induced toxic epidermal necrolysis. *Clin Dermatol*, 1998; 16: 399–408
- Saha K, Gupta AK: Toxic epidermal necrolysis: Current concepts in pathogenesis and treatment. *Indian J Dermatol Venereol Leprol*, 2000; 66: 10–17
- Downey A, Jackson C, Harun N, Cooper A: Toxic epidermal necrolysis: Review of pathogenesis and management. *J Am Acad Dermatol*, 2012; 66: 995–1003