

Stevens-Johnson syndrome with vulvar involvement: A case report and literature review

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ABSTRACT

Stevens-Johnson syndrome is a rare, life-threatening mucocutaneous condition causing necrosis and detachment of the epidermis. Vulvovaginal involvement, seen in up to 70% of affected women, can lead to painful chronic conditions such as adenosis, hematocolpos, and chronic pelvic pain. To date, there is no consensus regarding the optimal treatment of vulvovaginal involvement. In this case report, one case of Stevens-Johnson syndrome with vulvar and vaginal involvement is described, and the treatment options for this rare condition are reviewed.

1. Introduction

Stevens-Johnson syndrome (SJS) is a rare and life-threatening mucocutaneous condition characterized by extensive necrosis and detachment of the epidermis. It is commonly triggered by medications, including anti-epileptics, oxicam non-steroidal anti-inflammatory drugs (NSAIDs) (Piroxicam, Meloxicam, Isoxicam, etc.), and sulfonamide antibiotics, but can occasionally be related to infection or other causes. Certain HLA phenotypes such as HLA-B15 and HLA-A31 put patients at increased risk of developing SJS [1,2]. It can occur at any age and is more common in patients assigned female at birth [3]. The pathogenesis of SJS is incompletely understood and diagnosis is made primarily clinically but confirmed by biopsy. The incidence of SJS has been difficult to determine but it is estimated to affect between one and seven people per million in the general population each year, with a 1:2 female:male predominance [4].

Following a brief prodrome, patients with SJS start to develop skin lesions in the form of a painful erythematous rash [1]. This eventually progresses to extensive, full-thickness epidermal necrosis and sloughing [1]. SJS exists on a spectrum with toxic epidermal necrolysis (TEN), which is diagnosed when the skin involvement covers >30% of the patient's body surface area [1]. The mortality rate of SJS is approximately 30% [1]. Almost all patients experience mucous membrane involvement, particularly of the oral, ocular, and urogenital mucosa [1,2,5]. Up to 70% of patients with TEN can have acute vulvovaginal involvement [6].

The most important first measure of care is cessation of treatment with the triggering medication or agent. Supportive care is subsequently recommended for management of SJS as there is currently no consensus on the optimal treatment strategy. This may include pain relief, fluid replacement, supplemental nutrition, treatment for infection, and supplemental oxygen. Some patients may require treatment in a burn center. Recent advancements in SJS treatment, including treatment with corticosteroids, cyclosporine, and TNF- α antagonists, have reduced mortality rates. However, these advancements have come with the cost of more chronic complications, including chronic pain, long-term psychological complications, oral and dental sequelae, and blindness if ocular involvement is noted [1,2]. Gynecological complications include labial agglutination, introital stenosis, vaginal dryness, dyspareunia, urinary retention, hematocolpos, and vaginal adenosis [5,7,8]. Up to 28% of patients with toxic epidermal necrolysis may develop chronic vulvovaginal sequelae [6].

Despite the possibility of chronic complications, the high potential of vulvovaginal involvement, and the life-threatening nature of the condition, there is little consensus about prevention and treatment of gynecologic symptoms in patients with SJS/TEN [6,9].

Here, the case of a patient who presented with SJS with vulvar and vaginal involvement following treatment with lamotrigine is described.

2. Case Presentation

A 24-year-old nulliparous woman presented to the emergency

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department for a blistering rash involving her face, chest, and groin. She was admitted to the ICU for concern for SJS, which was later proven by biopsy. Three weeks prior to admission she had been started on lamotrigine for a mood disorder. The day before admission she noted a sunburn-like rash, which developed into a diffuse rash with bullae. On admission, she was noted to have approximately 60–70% of body surface involvement with 10–15% desquamation. She was given a course of infliximab and intravenous solumedrol.

On hospital day 4, the gynecology service was consulted due to vulvar and vaginal involvement. On exam she had a papular rash on the external genitalia with open, erythematous, desquamated areas noted upon separation of labia majora and near complete fusion of the labia minora (Fig. 1). An internal exam was unable to be performed due to labial agglutination. At this time, she was started on external Clobetasol cream daily by the gynecology service.

Two days later, on hospital day 6, there was an area of desquamation and a small labial opening (Fig. 2); there was concern that vaginal fusion or synechia may develop. At this point a vulvologist was consulted. A 25 mg hydrocortisone suppository was gently placed intravaginally and 2.5 mg hydrocortisone ointment was used to cover a 26 French renal dilator, which was placed intravaginally for 2 h.

The gynecology team recommended menstrual suppression via either Depo-Provera injection or leuprolide due to the risks of subsequent vaginal adenosis; however, there was concern that leuprolide might impact the patient's previously diagnosed mood disorder and that there was no unaffected skin for intramuscular Depo-Provera administration. Estrogen-containing methods were not favored due to immobility and risk of venous thromboembolism.

The following day, a 25 mg hydrocortisone suppository was placed intravaginally and a 28 French renal dilator was coated with 2.5 mg hydrocortisone ointment and placed vaginally for 2 h. After it was removed the labia were noted to be separated enough for an internal exam to be performed. On exam there were no vaginal adhesions and the cervix was able to be palpated. At this time, since the involvement only seemed to include the vulva and not the vagina, the decision was made to discontinue dilator therapy. From that point forward it was decided to continue twice-daily vaginal hydrocortisone suppository placement with Clobetasol ointment externally.

This regimen was continued for hospital days 8 through 11. On hospital day 12 this was changed to a hydrocortisone suppository placed only once per day with hydrocortisone ointment externally. A rolled piece of Vaseline-soaked gauze was placed between the labia minora to encourage continued labial separation and prevent re-agglutination (Fig. 3). On hospital day 16 the patient received Depo-Provera. On



Fig. 1. Vulvar presentation on hospital day 4.



Fig. 2. Desquamation on left side of labial majora (oval) and small labial opening (circle).

hospital day 16 she reported vaginal itching and nystatin was applied due to concern for a vaginal yeast infection.

Hospital day 17, the suppositories were discontinued, and the labia were able to be completely separated and internal exam revealed no adhesions (Fig. 4), although small desquamation persisted. The Vaseline-coated gauze was continued. On hospital day 18, due to concern for fungal infection, the patient was given intravenous fluconazole. On hospital day 20 she was discharged home with plans for outpatient follow-up.

Following her discharge, she was seen 3 weeks later for outpatient follow-up. On exam she had normal-appearing external genitalia and no vaginal sequelae (Fig. 5). Her skin was healing well without significant scarring.

3. Discussion

Vulvovaginal involvement can be present in up to 70% of SJS cases, and the long-term sequelae of vulvovaginal involvement can include labial scarring, agglutination, introital or vaginal stenosis, adenosis, hematocolpos, and inability to have sexual intercourse [9–11]. In the present case, the patient was a young, sexually active women with labial agglutination. Although the inciting medication had been stopped immediately upon recognition, the goal was to prevent permanent scarring of the labia. The challenge was determining best practices for management of this patient, as there are currently no guidelines on the management of vulvar or vaginal involvement of SJS.

The goal of gynecological intervention is to preserve vaginal function and decrease inflammation. Therefore, topical glucocorticoids are usually first the first line of intervention [12]. The risk of systemic absorption with topical steroids and subsequent infection and sepsis is unlikely [12] and high-potency steroids should be started immediately. In this patient, external Clobetasol cream was prescribed on the first day the gynecology team was consulted. However, after two days of treatment, the patient reported no improvement of symptoms. Due to concern for progressive worsening of vaginal fusion and inability to do a proper gynecological exam to determine the extent of vulvovaginal involvement, a shared decision between the gynecology team, patient, and the patient's family was made for more aggressive intervention.

Vaginal molds or dilators with steroids can help prevent labial and vaginal adhesions [10]. The goal was to prevent further vulvar scarring in this young, nulliparous patient who was sexually active. Therefore, a hydrocortisone suppository was placed intravaginally along with a renal dilator enveloped with hydrocortisone ointment for a few hours. Within one day, the folds of the vulva were able to be separated and an internal vaginal exam was performed. This revealed no involvement of the vagina, and the dilator therapy was discontinued. Once the labia minora were able to be separated, the rolled piece of Vaseline-soaked gauze was critical to encourage continued labial separation and prevent re-

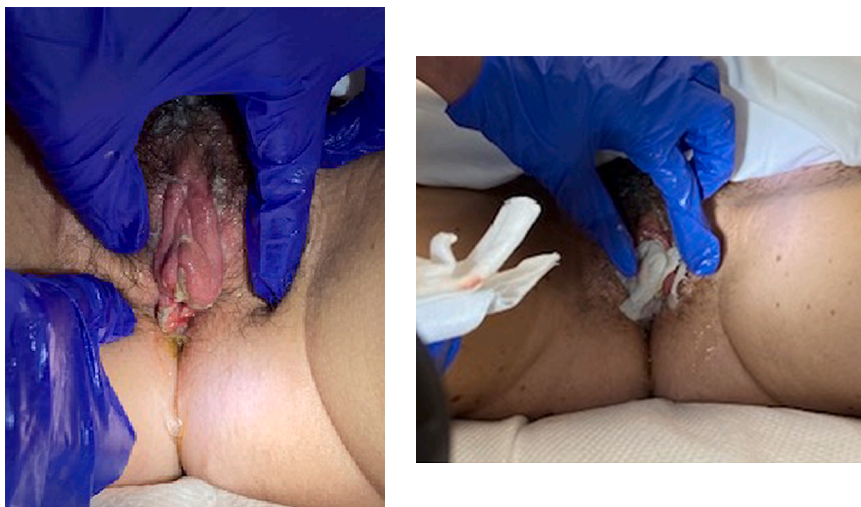


Fig. 3. A. Labia minora before rolled gauze placed. B. Labia minora with rolled gauze placed to maintain separation.



Fig. 4. Labia minora able to be completely separated by hospital day 17.



Fig. 5. Vulvar appearance 3 weeks after discharge.

agglutination as the healing process occurred.

The final goal was to suppress the patient's menstrual cycle to reduce the risk of adenosis. Case reports describe pathological examination of women who have had vaginal or vulvar involvement of SJS with adenosis [7,13]. Since vulvovaginal adenosis has the potential to transform

into squamous, mucinous, or clear cell carcinoma [14,15], it is important to suppress the patient's menses if there is labial stenosis [10]. Leuprolide is commonly used to create a hypoestrogenic environment and suppress menses [7]. However, leuprolide can cause changes in mood and behavior and was not the preferred treatment in this patient. Ultimately, Depo-Provera injection was chosen. However, it is important to counsel that the efficacy of Depo-Provera or oral contraceptive pills in preventing adenosis has not been shown yet [5].

4. Conclusion

Stevens-Johnson syndrome is a rare disease but can have a long-lasting impact on a person's physiological and psychological state. Therefore, it is crucial to act rapidly and involve a multidisciplinary team in the care of the patient. Vulvar and vaginal involvement is common in SJS and having a consensus for best practice for management will help guide gynecologists in the future.

Contributors

Jessie Hollingsworth contributed to writing the manuscript. Selena U Park contributed to writing the manuscript. Veena Bhagavathi contributed to writing the manuscript. Ashlee Green contributed photographs and to editing the manuscript. Nancy Philips (the attending vulvologist) cared for the patient, and contributed photographs and to editing the manuscript. All authors approved the final manuscript.

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Conflict of interest statement

The authors declare that they have no conflict of interest regarding the publication of this case report.

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