Stevens-Johnson Syndrome Secondary to Topical Ofloxacin

Corresponding Author: Stephen J. Carlan, e-mail: stevecarlan@gmail.com

Financial support: None declared
Conflict of interest: None declared

Patient: Female, 36-year-old
Final Diagnosis: Stevens Johnson syndrome
Symptoms: Nonspecific flu-like prodrome with fever and rash
Clinical Procedure: —
Specialty: General and Internal Medicine

Objective: Rare disease
Background: Stevens-Johnson syndrome (SJS) is a rare dermatologic disorder that is characterized by nonspecific flu-like prodrome with fever, malaise, myalgia, cough, rhinitis, and sore eyes, followed by a characteristic rash and mucocutaneous manifestations. It is triggered by medications in up to 80% of cases in adults. In each of these cases, the medication is oral or parenteral. Severe and progressive SJS can result in life-threatening complications. Adult-onset medication-induced SJS presents within 8 weeks of exposure to the offending substance, lasting 8 to 12 days. Recovery of denuded skin generally is complete within a month. There is no consensus on treatment, but supportive care with corticosteroids is often the initial intervention.

Case Report: A 36-year-old woman with a flare of allergic rhinitis and tearing resistant to over-the-counter options was treated with topical ophthalmic ofloxacin. She began experiencing a diffuse mucocutaneous rash, with oral desquamation, tongue swelling, vaginal desquamation, and rash of the palms and soles within 24 h, which suggested the possibility of SJS. A skin biopsy was obtained, and pathology confirmed this suspicion. She was treated with parenteral antibiotics, corticosteroids, and supportive care, and after 10 days was discharged from the hospital. She had a complete recovery in 30 days.

Conclusions: The clinical course of SJS induced by the ophthalmic application of medication can be just as severe as the oral or parenteral routes. This is, to the best of our knowledge, the first documented case of SJS being triggered by topical ofloxacin.

Keywords: Dermatology • Ofloxacin • Stevens-Johnson Syndrome

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/941992

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**Background**

Stevens-Johnson syndrome (SJS) is a rare and feared dermatologic disorder that is characterized by the sheet-like loss of denuded skin associated with a myriad of systemic symptoms. It is triggered by medications in up to 80% of cases in adults [1], and a small proportion of cases have been well-documented to be secondary to *Mycoplasma pneumoniae* and Herpes simplex infections [2]. No proximal cause can be found in a small percentage of cases.

In severe and progressive SJS, sheet-like loss of denuded skin can occur and result in life-threatening complications. In virtually all cases of adult-onset medication-induced SJS, the disorder appears within 8 weeks of exposure to the offending substance [3]. The acute phase of SJS typically lasts 8 to 12 days [4]. Supportive care with corticosteroids is often the initial intervention [5]. There currently remains no consensus on treatment. Treatment with cyclosporine and intravenous (i.v.) immunoglobulin has been described positively in the literature in recent years but remains controversial [6,7].

Despite its rarity, there are several specific drugs and drug classes that are classically considered high risk for inducing SJS, including allopurinol, aminopenicillins, cephalosporins, sulfonamide antibiotics, -oxicam nonsteroidal anti-inflammatory drugs, and a variety of antiepileptic drugs, such as carbamazepine, phenytoin, and phenobarbital [8,9].

It has not been until recent years that there have been reports of fluoroquinolone-induced SJS; the vast majority were secondary to oral ciprofloxacin use [10].

Here we present a 36-year-old female patient with a flare of allergic rhinitis and tearing resistant to over-the-counter options, which was ultimately treated with topical ofloxacin. This patient began experiencing a diffuse mucocutaneous rash with oral desquamation, tongue swelling, vaginal desquamation, and rash of the palms and soles, with concern for SJS. A skin biopsy was obtained, and the pathology results confirmed this suspicion. This is, to the best of our knowledge, the first documented case of SJS being triggered by topical ofloxacin.

**Case Report**

A 36-year-old female patient presented to the Emergency Department (ED) with a 1-day history of fever, lip swelling, conjunctival redness (Figure 1), rash over the palms (Figure 2), and blistering beneath her tongue (Figure 3). The patient had recently spent a week in Dubai. In addition to being diagnosed with COVID-19 on return, she had an exacerbation of her seasonal allergies. After developing symptoms consistent
with allergic rhinitis and tearing, she attempted to use over-the-counter eyedrops, which did not resolve her symptoms. She subsequently went to see her ophthalmologist, who prescribed ofloxacin ophthalmic solution for instillation into both eyes. Within 24 h, the patient’s symptoms progressed to blistering beneath her tongue (Figure 3), with a constellation of symptoms that included eye redness with blurry vision, desquamating oral rash with tongue swelling, vaginal eruption with discharge, diffuse cutaneous rash involving the chest, back, palms, soles, and fever.

Upon ED evaluation, she was found to be febrile, at 38.6°C, without airway compromise. Skin examination revealed desquamation and edema of the lips and oral mucosa. A petechial rash was noted on her palms. Bilateral conjunctival injections were noted. Neck swelling with bilateral cervical lymphadenopathy was appreciated. The patient had no abdominal, supra-pubic, or costovertebral angle tenderness. Blood, lesion, and urine cultures were obtained and were negative. Blood testing results for HIV, syphilis, herpes, and varicella were negative. Rubeola immunoglobulin M was negative. She underwent a punch biopsy of lesions on her back, with pathology results revealing vacuolar interface dermatitis, consistent with erythema multiforme, SJS, or toxic epidermal necrolysis, a more severe presentation that typically involves greater than 30% of the body surface area. Direct immunofluorescence was negative.

The rapid onset of systemic and mucocutaneous illness suggests that the route of exposure to the ofloxacin may have been an operative variable. Even though conjunctival instillation has not been reported as an antecedent event, it may be a strong initiator of the inflammatory cascade resulting in SJS.

What part her COVID-19 played in the development of SJS can only be speculated. Rashes described in COVID-19 generally appear as urticarial or morbilliform and are wholly dissimilar to the rash seen in this patient [12]. Additionally, despite a temporal association to COVID-19, the lesions from this rash were biopsy-proven to be consistent with mucocutaneous SJS lesions. The rapid onset of systemic and mucocutaneous illness suggests that the route of exposure to the ofloxacin may have been an operative variable. Even though conjunctival instillation has not been reported as an antecedent event, it may be a strong initiator of the inflammatory cascade resulting in SJS in select individuals.

FIGURE 3. Within 24 h after application of the ophthalmic ofloxacin drops, blistering beneath the tongue at the black arrow further illustrates the classical and extensive mucocutaneous involvement seen in Stevens-Johnson syndrome.

Discussion

SJS and toxic epidermal necrolysis are both conditions on the same spectrum of severe epidermolytic cutaneous reactions, with considerable overlap; so much so that one is seldom mentioned without the other. SJS is defined as the involvement of less than 10% of the body surface area of the skin, and toxic epidermal necrolysis is defined as the involvement of greater than 30% of the body surface area of the skin [11].

SJS usually begins with a nonspecific flu-like prodrome with fever, malaise, myalgia, cough, rhinitis, and sore eyes. Soon after these symptoms, cutaneous manifestations occur, which include Nikolsky-positive flaccid bullae, erosions, and erythematous macular rash involving mucosal surfaces and the face, trunk, and extremities. This is not unlike our patient, whose mucocutaneous involvement involved the lips and vagina and a macular rash on the palms and soles.

SJS secondary to topical medications appears to be a vanishingly small minority of cases, with the vast majority taken in a systemic fashion, such as orally or intravenously [9]. The diagnosis can be challenging since not all cases follow medication ingestion and the timing from exposure to disorder onset is variable. In addition, the order of presentation and spectrum of symptoms can differ, as was seen in our patient, who presented with concurrent mucocutaneous pathology and full-blown flu-like illness.

The Infectious Disease Department was consulted for evaluation and continued the aforementioned regimen to cover bacterial translocation from non-intact mucosa, and i.v. methylprednisolone was given. The burn team was consulted for wound care. The patient was treated and monitored inpatient for 10 days and followed up as an outpatient after discharge with the burn team. By day 20, the patient’s diffuse rash had resolved, and by day 30, the patient’s blisters and ulcers had healed.

She was started on i.v. vancomycin, i.v. piperacillin/tazobactam, and oral nystatin, empirically. The Infectious Disease Department was consulted for evaluation and continued the aforementioned regimen to cover bacterial translocation from...
Conclusions

This appears to be the first case of SJS following ophthalmic ofloxacin application. It is paramount that clinicians and other providers are aware that medication-induced SJS can be possible in patients who have received no oral or parenteral medication. Additionally, based on this single case, SJS from topical sources is just as severe as SJS from oral or parenteral sources. The treatment for topically induced SJS is unchanged and centers on supportive care and corticosteroids.

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References: