A diagnosis of Stevens-Johnson Syndrome (SJS) in a patient presenting with superficial keratitis

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A R T I C L E   I N F O

Purpose: To describe a case of Stevens-Johnson syndrome (SJS) diagnosed in a patient presenting with primarily ocular findings where SJS had not been initially suspected.

Observations: A 23-year-old female presented with a 2 day history of bilateral eye pain, conjunctival injection, decreased visual acuity, and photophobia in the context of a 4 day history of fever, headache, and sore throat. She was found to have bilateral superficial keratitis and treated for suspected early infectious keratitis secondary to extended contact lens wear. She returned the next day with worsening visual symptoms, a new macular rash over her upper torso, and new ulcerating lesions over her buccal and perioral tissue. The patient was diagnosed with SJS. She was successfully treated using systemic cyclosporine with antibiotics and steroid eye drops.

Conclusions and importance: Ophthalmologists may be the first physicians to diagnose SJS, a life-threatening condition that can initially present with non-specific viral prodromal symptoms and ocular signs alone. This case emphasizes the importance of considering a patient's entire clinical history, especially when the presentation is atypical and the diagnosis is not obviously apparent.

1. Introduction

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are thought to represent variants of the same severe immunologic mucocutaneous reaction characterized by blister formation, hemorrhagic erosions, and epidermal necrosis.1,2 Often triggered by an offending medication, symptoms typically begin 4–28 days after the drug is first introduced. Ophthalmologists rarely see undiagnosed SJS or TEN; primary care providers, emergency physicians, or consulted dermatologists usually identify the characteristic skin eruptions. However, nearly 45% of patients recall episodes of conjunctivitis up to 4 days before skin eruptions develop¹ and 60–71% of SJS cases have acute ocular involvement.³ Thus, with an appropriate level of suspicion, SJS and TEN may be first diagnosed by an ophthalmology service.

We report an unusual case of a patient diagnosed with SJS who initially presented with non-specific viral prodromal symptoms and bilateral superficial keratitis following a course of oral clindamycin.

2. Case report

A 23-year-old female was referred for an ophthalmology consultation following a two day history of bilateral conjunctival injection, decreased visual acuity, and photophobia. She described a four day history of non-specific viral prodromal symptoms that included a fever as high as 40 °C, headaches, and a sore throat. Her family physician had treated her systemic symptoms as a presumptive bacterial pharyngitis with cefixime 400 mg orally once daily. Serology was ordered to rule out infectious mononucleosis. Prior to her symptoms, she was healthy with no regular medications, no allergies, and no personal or family history of severe drug reactions. Her ocular history was significant for monthly soft contact lens use. Incident note was made of two separate antibiotics she had taken prophylactically during the past month following dental procedures.

On examination, her spectacle corrected visual acuity was 20/400 in her right eye with pinhole correction to 20/100, and 20/60 in her left eye with pinhole correction to 20/50. Intraocular pressures were normal and both pupils were equal and reactive to light. Slit lamp evaluation demonstrated moderate diffuse conjunctivitis with a
papillary reaction and no pseudomembranes in either eye. Her right cornea had a central 8 by 8 mm area of patchy, roughened epithelium with occasional bullae; fluorescein uptake was poor and there were no corneal infiltrates. The left cornea had a similar appearance over a smaller 3.5 by 7.5 mm area paracentrally. Her anterior chambers were deep and quiet and her crystalline lenses were clear. A dilated posterior segment examination was unremarkable. Given her history of extended contact lens use, she was diagnosed with early infectious keratitis manifesting as superficial keratitis. She was treated aggressively with topical moxifloxacin 0.5% drops every hour around-the-clock in both eyes and counseled to temporarily avoid contact lens wear. Follow-up was arranged for the next day.

When she was seen 24 h later, she had developed a new macular rash over her upper chest and back (Fig. 1a), as well as erosive lesions and some pustular lesions in her mouth, lips and perioral area (Fig. 1b). She denied any genital lesions and there were no targetoid lesions on her palms and soles. Her spectacle corrected visual acuity with pinhole had worsened to 20/150 and 20/200 in her right and left eyes respectively. Conjunctival injection was still moderate with no pseudomembranes; however, her corneas now demonstrated loose, full-thickness sloughing epithelium with exposed areas of Bowman’s membrane. Serology showed an elevated alanine aminotransferase (ALT) of 339 IU/L and a low white blood cell (WBC) count of 3.7*10^9/L (neutrophils 2.3*10^9/L, lymphocytes 1.1*10^9/L, and eosinophils 0.1*10^9/L).

Given the rapid progression of her constellation of symptoms, concern was raised for Stevens-Johnson syndrome (SJS) and recent medication usage was reviewed. Her dentist had prescribed amoxicillin and clindamycin 35 days and 17 days prior to her symptom onset, respectively. Cefixime had been prescribed two days after the onset of her non-specific viral prodromal symptoms. The time course suggested clindamycin as the likely culprit. Internal medicine and dermatology were urgently consulted.

She was admitted to hospital where skin biopsies were taken and she was started on oral cyclosporine 200 mg BID. Her loose corneal epithelium was debrided at the slit lamp. Bandage contact lenses were placed in both eyes and moxifloxacin 0.5% drops were administered every 3 h. During her hospitalization, her systemic symptoms improved considerably; this was attributed to the early introduction of cyclosporine. Skin biopsies disclosed interface lymphocytic dermatitis with many intraepidermal necrotic keratinocytes. The findings of transepidermal necrosis with an intact cornified layer (Figs. 2 and 3) were in keeping with a diagnosis of SJS/TEN. Serologic studies for Epstein-Barr virus (EBV), herpes simplex virus (HSV), hepatitis A, B, C, and human immunodeficiency virus (HIV) were negative.

On reassessment 3 days later, her spectacle corrected pinhole visual acuity had improved to 20/50 and 20/60 in her right and left eyes respectively. The cornea had reepithelialized and showed only residual punctate epithelial erosions. Her conjunctivae were less injected and pseudomembranes had developed in the inferior conjunctival fornices. These were removed with a cotton-tipped applicator. Moxifloxacin drops were tapered to every 4 h and prednisolone acetate 1% drops were added every 3 h.
Our patient was discharged from hospital in stable condition after 4 days with significant improvement in the appearance of her skin and mucous membranes. ALT had decreased to 99 IU/L. On reassessment six days after discharge, her spectacle corrected pinhole visual acuity had further improved to 20/30 in her right eye and 20/25 in her left eye. She had only minimal conjunctival injection with persistent corneal punctate epithelial erosions.

3. Discussion

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare entities that occur in 1–2 individuals per million per year in the general population, or 1–2 per 1000 for those infected with HIV. The two entities are a spectrum as defined by the amount of total body surface area affected: SJS when there is less than 10% involved, an intermediate form of SJS/TEN with 10–30% involvement, and TEN where there is greater than 30% involvement. Our patient had less than 10% total body surface area involved, thereby classifying her as SJS. Mortality rates can be high, ranging from less than 5% in SJS to 30% in SJS/TEN and TEN. Thus, it is important to quickly diagnose and treat SJS and TEN to limit mortality and sequelae.

Stevens-Johnson syndrome rarely presents initially to ophthalmology with primary ocular findings; however, 45% of patients recall episodes of acute conjunctivitis starting from hours up to four days before the characteristic skin eruptions. Thus, ophthalmologists can play an integral role in the diagnosis of SJS. Our case emphasizes the importance of considering SJS in a patient presenting with systemic symptoms and ocular involvement following drug exposure.

Rapid diagnosis and intervention is crucial as patient prognosis improves with early discontinuation of the inciting agent. Furthermore, while our patient fortunately did not require admission to a burn unit, the necessity for prompt diagnosis is evident from the finding of the direct correlation between patient survival and time to admission to a burn unit. Early diagnosis also allows for early systemic intervention. Our patient's condition improved on systemic cyclosporine; other reports have shown similar benefits of cyclosporine in the management of SJS/TEN.

Possible acute ocular findings of SJS include conjunctivitis, corneal or conjunctival defects, corneal perforation, pseudomembrane formation, and lid margin keratinization. Chronic sequelae such as lid and ocular surface keratinization, aqueous tear deficiency, and persistent corneal epithelial defects can lead to reduced best-corrected visual acuity (17%), dry eye (32%), and corneal pannus (19%). Our patient developed ocular surface dryness; as a result, preservative-free artificial tears became an important component of her treatment plan. Given the significant vision threatening sequelae that can develop, continued follow-up during both the acute phase and long-term is integral for vision preservation in patients with SJS.

Clindamycin is a rare trigger for SJS. To date, there have only been 5 previous reports of SJS or TEN caused by clindamycin. Drugs typically associated with SJS and TEN include certain antiepileptics (e.g. carbamazepine, lamotrigine, oxcarbazepine, and phenytoin), certain antibiotics (sulfonamides in particular), oxicam NSAIDs, and allopurinol. To the best of our knowledge, our case represents only the sixth published instance of SJS caused by clindamycin.

4. Conclusions

Ophthalmology can play an integral role in limiting life- and vision-threatening complications of Stevens-Johnson syndrome (SJS) through proper and timely diagnosis and management. This case demonstrates the importance of considering and accounting for a patient's entire clinical presentation, especially for atypical features and during instances of diagnostic uncertainty. Finally, despite being rare, SJS should be considered in a patient presenting with an adverse reaction to clindamycin.

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Conflicts of interest

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

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