Visual Diagnosis: Rash, Eye Pain, Lesions in an Adolescent
Sarah Powers and Gina Carter-Beard
Pediatrics in Review 2010;31:e86
DOI: 10.1542/pir.31-12-e86

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://pedsinreview.aappublications.org/content/31/12/e86
Rash, Eye Pain, Lesions in an Adolescent

Sarah Powers, MD,* Gina Carter-Beard, MD†

Presentation

A 17-year-old boy presents to his primary care practitioner with a 3-day history of rash, bilateral eye irritation, and sores in his mouth and on his genitals. He had been seen in the emergency department approximately 1 week ago for fever and a sore throat. A rapid streptococcal antigen test was positive at that time, and he was started on oral azithromycin therapy. Four days later, he developed facial swelling, eye redness, and “hives,” appearing initially on his hands, then spreading to his legs and feet. Although his sore throat resolved, new and different oral lesions appeared, and his lips became chapped and painful, prompting him to go to an urgent care clinic, where his azithromycin therapy was discontinued and he was started on oral prednisone and diphenhydramine. However, his skin lesions and eye pain continued to worsen, and sores appeared on his genitals. When he developed dysuria, he presented to his primary care physician for additional evaluation.

The patient reports a history of allergy to penicillin, manifesting as hives in the past. Except for this past week, he takes no medications. There is no family history of skin disease. He is a sophomore in high school and smokes a half pack of cigarettes daily. He acknowledges occasional binge drinking and daily marijuana use but denies the use of other illicit drugs. He has been sexually active since the age of 16 years and has had many female partners, including some intercourse without protection, but denies any history of sexually transmitted infection.

Physical examination reveals an alert, thin, but well-nourished adolescent male. His temperature is 37.0°C, respiratory rate is 18 breaths/min, oxygen saturation is 100% on room air, heart rate is 65 beats/min, and blood pressure is 134/63 mm Hg. His weight is 58.7 kg (26th percentile for age). Examination of his head, ears, nose, and throat reveals dry, peeling, bleeding lips with erosions (Fig. 1); erythema of the soft palate with tonsillar erosions and exudates (Fig. 2); and several palpable 5-mm nontender bilateral submandibular lymph nodes. His conjunctivae are injected. Skin examination shows

*Department of Pediatrics, University of New Mexico School of Medicine, Santa Fe, NM.
†Doernbecher Children’s Hospital, Oregon Health & Science University, Portland, Ore.
scattered annular vesicular lesions (5 to 7 mm in diameter) with surrounding erythema over the palms and dorsal aspects of his hands (Fig. 3). Similar lesions are present on his forearms and the plantar aspect of his right foot. Examination of his genitourinary system reveals a 2-cm erythematous desquamated area surrounding the urethral meatus (Fig. 4) and scattered 2- to 3-mm vesicular lesions on his penis and scrotum (Fig. 5). The remainder of the examination findings are unremarkable.

A complete blood count demonstrates a hemoglobin of 14.3 g/dL (143 g/L); hematocrit of 41% (0.41); and white blood cell count of $13.9 \times 10^3/\mu L$ ($13.9 \times 10^9/L$) with 90% neutrophils, 8% lymphocytes, and 2% monocytes. The platelet count is $455 \times 10^3/\mu L$ ($455 \times 10^9/L$). Serum electrolyte, blood urea nitrogen, creatinine, alanine transaminase, and aspartate transaminase values are normal, but the glucose is slightly elevated at 111 mg/dL (6.2 mmol/L). A urine drug screen is positive for cannabinoids but negative for other illicit substances. Laboratory evaluation for sexually transmitted diseases, including human immunodeficiency virus, syphilis, hepatitis C, Chlamydia, and gonorrhea, is negative.

A punch biopsy of a skin lesion (Fig. 6) confirms the diagnosis.
Diagnosis: Stevens-Johnson Syndrome

A clinical diagnosis of Stevens-Johnson syndrome (SJS), based on the targetlike skin lesions and oral mucosal involvement, was confirmed by punch biopsy of one of the hand lesions, which revealed necrosis and vacuolar change along the epidermal basal layer with adjacent subepidermal vesicle and perivascular lymphocytic infiltrate, histologic findings consistent with SJS.

Of note, the history of unprotected sexual activity plus the appearance of palmar and urethral lesions strongly suggested secondary syphilis in the differential diagnosis.

Discussion

SJS is one part of a spectrum of severe cutaneous reactions characterized by disseminated skin and mucous membrane lesions induced by exposure to drugs or infections. Clinically, this disorder presents as multiple target-shaped erythematosus macules, with or without epidermal detachment and necrolysis. SJS lesions can occur anywhere on the skin, involving up to 10% of the total body surface area. From 92% to 100% of individuals who have SJS experience involvement of the mucous membranes, with two or more mucosal surfaces usually affected. SJS typically is preceded by a prodromal phase consisting of fever, arthralgia, malaise, and myalgia.

Included in this spectrum of severe cutaneous reactions are toxic epidermal necrolysis (TEN) and, in the past, erythema multiforme (EM). However, the World Health Organization has formally distinguished EM from SJS and TEN, placing it in a separate category defined by its relatively benign nature and lack of mucosal involvement. TEN is a similar type of eruption that has more extensive skin and mucosal involvement and a more rapidly progressive course that involves exfoliation of the epidermis, producing a positive Nikolsky sign (detachment of epidermis with the application of lateral pressure). The Nikolsky sign also may be seen in SJS to a lesser extent. By definition, SJS must involve less than 10% of the body surface area, TEN must involve more than 30% of the body surface area, and SJS/TEN overlap defines involvement between 10% and 30% of body surface area (Table). TEN typically has more systemic involvement than SJS, and patients may exhibit anemia, lymphopenia, neutropenia, and mildly elevated serum liver enzyme values. Because of the more extensive systemic involvement, TEN has a significantly higher mortality rate than SJS (approximately 40% versus 5%), typically due to sepsis from bacterial entry into exposed dermis.

SJS occurs more commonly than TEN, with an estimated incidence of 1.2 to 6 cases per million annually. There is an equal female-male distribution among children, although the syndrome is more common in females among adults. Approximately 15% of cases are caused by infections, most commonly due to *Mycoplasma pneumoniae* and herpes simplex types 1 and 2. Another one third to one half of cases are attributed to drug exposure, with the most commonly implicated drugs including antibiotics (particularly sulfonamides, cephalosporins, and quinolones); antiepileptic drugs, including carbam-
azepine, phenobarbital, and phenytoin; and oxicam non-steroidal anti-inflammatory drugs (NSAIDs). Although cases of SJS triggered by azithromycin have been reported in children and adults, azithromycin is a rare cause of this disorder.

The pathophysiology of SJS and TEN is not known definitively, but proposed mechanisms include immunologic reactions, reactive drug metabolites, and interactions between these two mechanisms. Features supporting the role of the immune system in these disorders are an immune-mediated keratinocyte apoptosis that precedes the epidermal detachment and an infiltration of the epidermis with activated lymphocytes and macrophages. Some evidence suggests that patients who have SJS and TEN may have an altered ability to metabolize the drugs, leading to increased production of reactive metabolites that cause SJS or TEN. It is likely that interaction between both of these factors may play a role, with epidermal necrosis mediated by an immune reaction to reactive drug metabolites adhering to epidermal cells.

Other disorders to consider in the differential diagnosis include toxic shock syndrome and staphylococcal scalded skin syndrome. Exfoliative erythroderma, paraneoplastic pemphigus, and acute exanthematous pustulosis also can cause mucocutaneous lesions that can be confused with SJS or TEN. Skin biopsy is helpful for definitive diagnosis; full-thickness epidermal necrosis is present in SJS and in TEN but not in the other disorders.

**Management**

The standard of care for SJS is supportive therapy, including close monitoring of fluid and electrolyte status, wound care to prevent infection, nutrition support, and pain management. Mucosal involvement can lead to urologic and ophthalmic complications, and appropriate specialists should be consulted if these complications develop. The use of systemic corticosteroids is controversial. Although some have advocated their use early in the course of drug-induced cases, evidence from retrospective studies suggests that corticosteroids may not only fail to improve the prognosis but might increase patient susceptibility to sepsis and gastrointestinal hemorrhage. Off-label use of human immune globulin intravenous (IGIV) has not yet been studied in a well-controlled, prospective, multicenter trial but has been described in a number of case reports. Such therapy appears to result in decreased blister formation and faster recovery with minimal adverse effects. The typical dose of IGIV is 0.5 to 1.0 g/kg administered over 3 days.

**Patient Course**

The patient was admitted to the hospital and discharged after 24 hours, with instructions to complete the 5-day course of oral prednisone he had started before admission. Because of the association between SJS and infection, titers for *Mycoplasma* and herpes simplex virus types 1 and 2 were drawn, all of which were negative for acute infection. However, his lesions continued to worsen (Fig. 7), limiting his intake of food and liquids and necessitating readmission 3 days after discharge. At that time, clinicians decided to add IGIV at a dose of 1.0 g/kg divided over 3 days to the symptomatic treatment of his pain. Following IGIV administration, he improved significantly and was discharged from the hospital. At follow-up evaluation 1 week later, his lesions had resolved almost completely.

**Conclusion**

SJS is part of a spectrum of skin disorders, including TEN, that should be suspected in a child who has fever and mucocutaneous blistering lesions developing soon after recent drug or infectious exposure. Among the common infectious causes for SJS are *M pneumoniae* and herpes simplex type 1 or 2. Drugs frequently implicated in the development of SJS include antibiotic and antiepileptic medications and NSAIDs. Treatment of SJS is primarily supportive, including hospitalization and IGIV therapy for severe cases.

**Suggested Reading**

Auquier-Dunant A, Mockenhaupt M, Naldi L, et al. Correlations between clinical patterns and causes of erythema multiforme majus, Stevens-Johnson syndrome, and toxic epidermal necro-


---

HealthyChildren.org Parent Resources from AAP

KidsDoc Symptom Checker

http://www.healthychildren.org/symptom-checker