

Intravenous Immunoglobulin Therapy for Stevens-Johnson Syndrome

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ABSTRACT: Stevens-Johnson syndrome (SJS) is an acute mucocutaneous disorder that can be associated with considerable morbidity. Several previous reports, all involving either adults with acquired immunodeficiency syndrome or children, suggest that intravenous immunoglobulin may be an effective treatment for SJS. We report a case of SJS in an immunocompetent adult whose condition improved dramatically after therapy with intravenous immunoglobulin.

STEVENS-JOHNSON SYNDROME (SJS) is an uncommon mucocutaneous disorder usually attributed to a drug exposure or infection. Treatment is primarily supportive; some authors advocate corticosteroid therapy,¹ while others argue against it,² and few data support other therapeutic modalities. Administration of intravenous immunoglobulin for SJS has been reported in three pediatric cases^{3,4} and in two adult cases related to AIDS,⁵ but not for an immunocompetent adult. We report the case of a 27-year-old immunocompetent woman successfully treated with intravenous immunoglobulin for SJS associated with azithromycin and trimethoprim-sulfamethoxazole therapy.

CASE REPORT

A 27-year-old woman was admitted with dysphagia, fever, erosive stomatitis with drooling, and an erythematous, pruritic cutaneous eruption. Four days before admission, sore throat and fever had developed. She went to an emergency department at another hospital and was given azithromycin; the pharynx was not cultured. Two days later, the patient had generalized pruritus and conjunctivitis. She returned to the emergency department and azithromycin therapy was discontinued. The next day, she came to our emergency department with a truncal rash, coated tongue, fever, and progressive dysphagia, and was admitted with a diagnosis of presumed drug reaction to azithromycin. In addition, she had taken trimethoprim-sulfamethoxazole twice daily for several days for a urinary infection 14 days before admission. She had no known previous drug allergies.

Blood pressure was 102/84 mm Hg, pulse rate 150/min and regular, and temperature 103.4° F. The patient was in

moderate distress, with drooling and drainage from crusted lesions around the mouth and lips. She had injected conjunctivae with exudates. The tongue was coated with white plaques, and the gums and buccal mucosa were ulcerated. There was uvular edema and tonsillar enlargement without exudates. An erythematous cutaneous eruption consisting of confluent patches and plaques extended from neck to umbilicus, but spared the extremities. All blood test results were normal, and throat and blood cultures obtained on admission were negative for organisms.

Methylprednisolone (125 mg intravenously [IV] every 6 hours) and diphenhydramine (25 mg intramuscularly every 6 hours) were started. Because of high fever, systemic toxicity, and inability to exclude sepsis on admission, the patient received a single dose of IV ceftriaxone. During her first 48 hours in the hospital, bullous and necrotic lesions of the skin developed. An ophthalmologist noted diffuse corneal ulceration. The oral involvement progressed, with increasing odynophagia, hypersalivation, and erosive stomatitis. A skin biopsy confirmed the eruption as erythema multiforme major.

On the third hospital day, there were additional necrotic plaques and patches with bullae at areas of skin contact. A dermatologist recommended discontinuing all systemic medications (including methylprednisolone, of which she had received 6 doses by that time) and giving a dose of IV immunoglobulin (Polygam) at 1 g/kg (total dose, 60 g). On day 5, there was minimal improvement, and a second infusion of 60 g was given. Within 24 hours of the second dose, the skin and mucous membrane lesions improved dramatically. The patient was discharged on day 14. One year later, she remained well with no recurrences.

DISCUSSION

The etiology of SJS is frequently unknown, but many cases are associated with recent drug exposure or infection with pathogens such as herpes simplex virus or *Mycoplasma pneumoniae*. Our patient took azithromycin several days before the eruption and trimethoprim-sulfamethoxazole about 2 weeks before the eruption, without documentation of an infectious agent at either time. While the close temporal

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relationship suggests that azithromycin may be responsible in this case, a role for trimethoprim-sulfamethoxazole or infection remains possible. Sulfonamides are frequently associated with SJS, but we are unaware of previously reported cases of azithromycin-associated SJS.

Treatment options for SJS are limited and controversial.² Corticosteroids are commonly used,¹ but our patient had no obvious early response to high-dose corticosteroids. Case reports describe the use of cyclosporine A for severe toxic epidermal necrolysis (TEN),⁶ a disorder considered by some authorities to be on a spectrum with SJS.⁷ A recent report documents that early withdrawal of a drug causing SJS or TEN—particularly a drug with a short half-life—may improve outcome.⁸

We found three reports of therapy with intravenous immunoglobulin for SJS. Moudgil et al³ described two children with SJS associated with cefixime, and Amato et al⁴ described a child with phenobarbital-associated SJS. Sanwo et al⁵ reported two cases of SJS in adults with AIDS, after exposure to dapsone in one and trimethoprim-sulfamethoxazole and sulfadiazine in the other. Among these five patients, one received a single large dose of intravenous immunoglobulin (2 g/kg), and the other four received multiple smaller doses (0.4 to 0.5 g/kg). In addition, Swiss researchers recently described 10 patients with TEN treated with intravenous immunoglobulin.⁹ In each of these cases, as in our case, clinical improvement appeared temporally related to immunoglobulin therapy. However, it remains possible that our patient's improvement was spontaneous or due to corticosteroids.

Although the pathogenesis of SJS is not completely understood, considerable evidence indicates that it is an immune-mediated disorder.^{2,5} Intravenous immunoglobulin has a number of immunomodulatory effects, including blockade of reticuloendothelial Fc receptors, inhibition of complement-mediated damage, modulation of cytokines, and neutralization of circulating autoantibodies or antigens.¹⁰ Precisely which of these effects are primarily operative during intravenous immunoglobulin therapy for SJS is unclear.

Clinicians should be aware of several important caveats about the use of intravenous immunoglobulin. First, it is expensive—currently \$50/g to \$60/g in our hospital pharmacy. Second, it is occasionally associated with serious toxicity, including renal failure, aseptic meningitis, and anaphylaxis; hematologic and dermatologic adverse effects have also been described.¹⁰ Third, as a human plasma product it carries a potential risk for transmission of infectious agents.

In conclusion, to our knowledge this is the first reported case of an apparent response to intravenous immunoglobulin in an immunocompetent adult with SJS. Because we cannot be certain that the patient's response was solely or partially due to intravenous immunoglobulin, more experience is necessary before one can assume with confidence that this therapy favorably alters the natural history of SJS.

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