By Matthew Smelik, MD

Stevens-Johnson Syndrome: A Case Study

Abstract

Physicians writing prescriptions for their patients must warn them about possible side effects. One such potential complication of drugs—including tetracycline—is Stevens-Johnson syndrome, a potentially fatal condition that manifests mainly on the skin and mucosal surfaces but also affects other vital organs. Many types of therapy have proved efficacious for treating the syndrome, but use of steroid agents for this purpose remains controversial. Care for patients with Stevens-Johnson syndrome consists of treating the presenting symptoms.

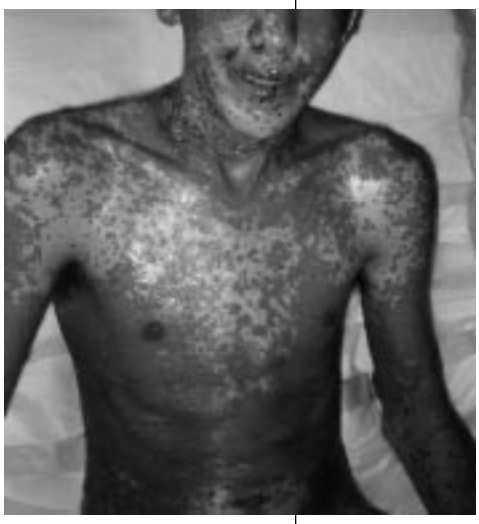
Introduction

Stevens-Johnson syndrome, otherwise known as erythema multiforme majus, is thought to represent a continuum of disease, the most benign type of which is erythema multiforme, whereas toxic epidural necrolysis is the most severe.[1] The condition was first described in 1922 by Stevens and Johnson as a febrile illness with stomatitis, purulent conjunctivitis, and skin lesions.[2] The syndrome is generally described as vesiculobullous erythema multiforme of the skin, mouth, eyes, and genitals.[3]

Case Report

A 14-year-old male patient presented to the emergency department complaining of four days of increasing dysphagia, dysuria, photophobia, and a macular rash extending from the trunk toward the extremities. The only medication used by the patient was tetracycline, which he had been taking for two weeks as treatment for facial acne. Vital signs were normal except for a temperature of 103.1°F. He appeared ill and had copious amounts of ocular drainage as well as small vesicles on the nasal and oral mucosa. An erythematous rash on his chest coalesced on the trunk with many small vesicles, some forming bullae. Vesicles were also present on the penis and scrotum.

The white blood cell count was slightly elevated at 11.7×10^9/L. Blood, herpes, and mycoplasma cultures as well as results of both rapid plasma reagin test and anti-DNA test were negative; and results of a skin biopsy were consistent with Stevens-Johnson syndrome. The presumptive cause was tetracycline. Empirical therapy with acyclovir was started but was discontinued after results of herpes culture proved negative. A regimen of 60 mg prednisone given intravenously twice daily was also started. When the oral lesions became so painful that the patient could not swallow his own saliva, a regimen of total parenteral nutrition was started, and the patient was given a patient-controlled anesthesia pump for administration of morphine. As the vesicles spread, they coalesced into larger bullae and sloughed off. The skin lesions were treated twice daily with a mixture of urea and triamcinolone in a lotion base. Multiple chest x-ray films showed no pulmonary involvement. Because of his need for increasing wound care, the patient was transferred to the intensive care unit. Ophthalmologic and urologic consultation was obtained to address ocular and urethral symptoms.



Erythematous rash

The area of denuded skin increased, and this development required even more labor-intensive treatment; the patient was therefore transferred to the county burn unit for wound management. His condition improved during the next two weeks, and he eventually recovered with minimal scarring on the back. Follow-up continued on an outpatient basis in the ophthalmology, dermatology, and urology departments.

Discussion

Incidence and Course of Disease

Stevens-Johnson syndrome occurs most often in children and young adults.[3] Incidence ranges from 1.2 to 6 cases per million per year; the condition is fatal in 5% of treated cases and in 15% of untreated cases.[4] Stevens-Johnson syndrome can be preceded by a prodrome consisting of fever, malaise, sore throat,

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nausea, vomiting, arthralgias, and myalgias.[5] This prodrome is followed within 14 days by conjunctivitis and by bullae on the skin and on the mucosal membranes of the mouth, nares, pharynx, esophagus, urethra, and vulvovaginal as well as anal regions.

Stevens-Johnson syndrome commonly affects multiple organs, and esophageal strictures develop in some patients.[6] Ocular complications occur in about 70% of patients with Stevens-Johnson syndrome.[7] Photophobia and a purulent form of conjunctivitis may be present initially, but corneal ulcerations and anterior uveitis can develop. Secondary infection, corneal opacity, and blindness can follow.[5] Pulmonary involvement may first appear as a harsh, hacking cough,[3] and chest x-ray films may show patchy areas of tracheal and bronchial involvement. The stomach and spleen can also be affected, and renal complications can occur in the form of acute tubular necrosis.[5]

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Etiology

Medications appear to be the most common cause of Stevens-Johnson syndrome and have been implicated in as many of 60% of cases studied.[5] Short courses of sulfonamide, aminopenicillin, quinolone, and cephalosporin drugs all increase risk of Stevens-Johnson syndrome.[8] Longer-term therapy with anticonvulsant agents, oxicam, nonsteroidal antiinflammatory drugs (NSAIDs), or allopurinol has also been named as a possible cause of Stevens-Johnson syndrome.[8] Even some chemicals, such as silver nitrite present in a wound dressing, have been implicated.[9] Although many medications have been blamed, some drugs administered for prodromal viral syndromes might have been falsely accused of causing Stevens-Johnson syndrome.

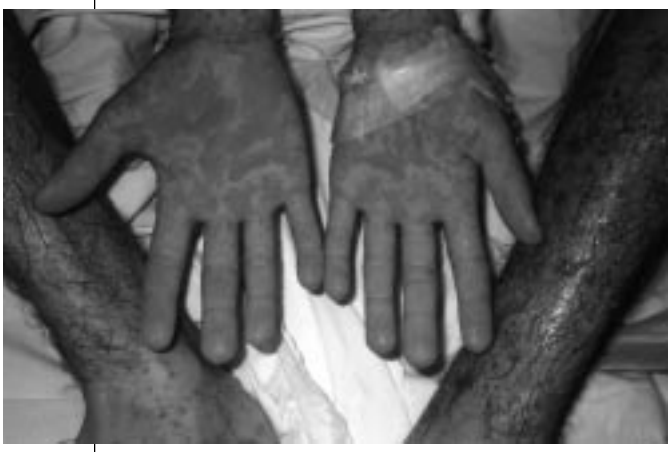
… in up to half of cases, no known cause can be found.

Stevens-Johnson syndrome also has been linked to herpes simplex virus, mycoplasma bacterial species, and measles vaccine.[10] Neoplasms and collagen diseases have also been pointed out as possible causes.[5] However, in up to half of cases, no known cause can be found.[5]

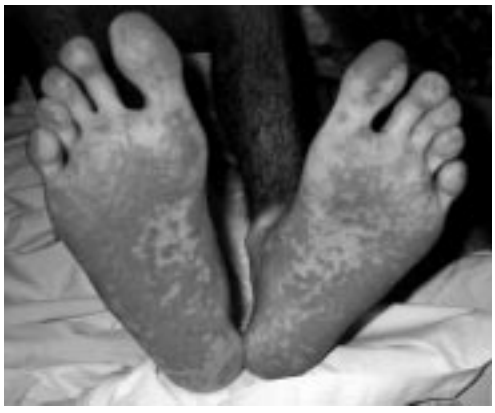
Treatment

Treatment for Stevens-Johnson syndrome is as diverse as the symptoms but should begin by withdrawing any offending agent identified. Many skin lesions can be treated with any of various topical mixtures, such as wet Burrow's compresses.[11] However, extensive skin involvement requires the staffing provided by a major burn unit. Treatment consists of warming the environment, increasing caloric intake, preventing superinfection and sepsis, and correcting electrolyte disturbance.[12] Affected patients and their first-degree relatives should be instructed to avoid any identified drug or chemical that may be responsible.[12]

Ocular involvement can be treated with topical corticosteroid agents, artificial hydration, and antibiotic agents when indicated. Pain from oral lesions may be lessened by rinsing with viscous lidocaine. A 50% water-to-hydrogen peroxide mixture can be used to remove necrotic buccal tissue. Antifungal and antibiotic agents should be used for superinfection.[11] Balloon dilatation is sometimes indicated for treatment of esophageal strictures.[13]



Erythematous rash in progressed stages.



Oral or intravenous use of steroid agents has been controversial. Many studies showed beneficial effects of using steroid agents in adults[14,15] and in children.[16] One study[17] suggested that mild to moderate disease can be managed with corticosteroid agents on an outpatient basis. Habif[3] mentioned that other studies suggest no benefits with steroid use and that others suggest that systemic steroid use might be associated with delayed recovery and clinically significant side effects. Because of many possible causes and varying degrees of severity, testing of steroid use is extremely difficult.

Review of the medical literature showed no studies showing the efficacy of systemic acyclovir therapy used in herpes-induced Stevens-Johnson syndrome. One small study on prepubertal children showed that erythema multiforme was unresponsive to topical acyclovir.[18]

Although mild forms of erythema multiforme majus may resolve in two to three weeks, recovery from Stevens-Johnson syndrome may require two to three months, depending on the number of organs affected and the severity of disease.[3]

Conclusion

Stevens-Johnson syndrome is a potentially fatal multiorgan disease with a strong etiologic link to some medications. Physicians must therefore consider Stevens-Johnson syndrome as a potential complication of treatment, especially when use of medication is questionable. The multiorgan aspect of the condition is best addressed by early involvement of medical specialists. Treatment with steroid agents may be helpful, but this option remains controversial. Affected patients and their first-degree relatives should be instructed to avoid any identified drugs or chemicals that may be responsible. ❖

Acknowledgment

The Kaiser Permanente Direct Community Benefit Investment Program provided research support.

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