

# Erythema Multiforme: Case Report and Discussion

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Erythema multiforme may be placed on a disease continuum that includes Stevens-Johnson syndrome and toxic epidermal necrolysis. It was first described in 1866 by Hebra as a skin disease with symmetrically distributed red papules, evolving within several days to form annular or iris-like shapes or blisters. The term multiforme described this evolution of primary lesions into different forms. In 1922 Stevens and Johnson described a febrile illness with stomatitis, purulent conjunctivitis, and skin lesions similar to those of erythema multiforme, which has become known as Stevens-Johnson syndrome or erythema multiforme major.<sup>1,2</sup> Toxic epidermal necrolysis, with severe exfoliation of the skin and mucous membranes and a high rate of mortality, is considered by many sources to be at the most severe extreme of this disease spectrum.

## Case Report

An 18-month-old boy was brought to the emergency department with worsening generalized body rash. There was no complaint of fever, lack of oral intake, itchiness, or ocular involvement. One week earlier he had been seen for presumed otitis media and given a prescription for amoxicillin. Five to 6 days after starting the medication, he began to develop an erythematous rash that began on his arms and legs. Two days later the rash was evident on his palms and soles, as well as truncal area. Initially the rash was specifically described as beginning as small areas of redness, which within days became raised and enlarged and then developed surrounding lighter layers and central areas of paleness.

Upon examination the child was mildly fussy, but consolable. His temperature was 98.8°F, and his blood pressure and pulse were stable. His left

tympanic membrane was clear and the right was dull and erythematous. His sclerae and conjunctivae were without any lesions. His nose and throat were clear, and there were no lip or oral mucosal lesions. Heart, lung, and abdominal examination results were all unremarkable. His skin had multiple lesions on the extensor surfaces of all extremities, the chest, the back, and the face. Some of the lesions were solid raised erythematous areas, and others were target-like lesions with central pallor, raised erythematous borders, and surrounding layers of lighter erythema.

Complete blood cell count was within normal limits, and no other laboratory data were obtained. The child's condition was diagnosed as erythema multiforme. His mother was told to stop the amoxicillin and was given a prescription for cefixime. He was also given a prescription for an oral prednisone solution 1 mg/kg. Instructions were given for the child to return if any oral or ocular lesions were noted, if oral intake ceased, or if the rash developed any signs of superinfection. The child was seen 1 week later with good resolution of symptoms. Lesions were sparse with mild resolving erythema and hyperpigmentation. During an examination 1 month later, no skin lesions were observed.

## Discussion

The causes of erythema multiforme and its disease spectrum are numerous. Herpes simplex virus, *Mycoplasma pneumoniae*, and drug reactions are the most common. Herpes simplex virus accounts for more than one half the cases of erythema multiforme. Both type 1 and 2 infections are associated, and repeated episodes of secondary erythema multiforme associated with recurrent herpes simplex virus are common. Mycoplasma infection is the most commonly recognized bacterial infection associated with erythema multiforme and can cause the disease 1 to 3 weeks after the respiratory illness. Drug-associated erythema multiforme is common with the use of antibiotics, especially penicillins and sulfonamides. It can be seen 1 to 3

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weeks after drug therapy is started.<sup>3</sup>

Other less common causes of erythema multiforme include vaccinia, bacteria, fungi, drugs, irradiation from radiographic studies, malignancy (carcinomas and lymphomas), and certain collagen-vascular diseases (lupus erythematosus, dermatomyositis, and periarteritis nodosa).<sup>2,4</sup>

Erythema multiforme is more common in male patients and in those aged less than 20 years, and it might be related to seasons because there is higher incidence in some months of provoking agents, such as mycoplasma and herpes simplex virus infection.<sup>5</sup>

### ***Diagnostic Evaluation***

Because there are serious sequelae involved in the most severe manifestations of this disease spectrum, it is important to recognize the clinical signs and symptoms of various forms of the disease so that a prompt diagnosis can be made and a proper treatment regimen can be started.

The characteristic rash of erythema multiforme is often preceded by nonspecific prodromal symptoms, suggesting an infection of the upper respiratory tract. The hallmark target or iris lesions occur 7 to 10 days later, symmetrically on the extensor surface of limbs, the dorsum of hands and feet, and the palms and soles. Lesions begin as areas of circumscribed erythema with clearly defined margins, which then become raised. They grow eccentrically, and after 24 to 48 hours become several centimeters in diameter. Days later they form a peripheral ring of lighter color and the center then flattens and becomes a cyanotic red color, thus assuming a target or iris-like appearance. Lesion centers can also form blisters with peripheral microvesicles (in herpes-related infections). Five to 7 days later the lesions retract and heal completely with only transitory hyperpigmentation. Subjective symptoms are limited only to a burning sensation. Prognosis is very good with complete healing in all cases and a recurrence rate of 22 to 37 percent.<sup>5</sup>

In Stevens-Johnson's syndrome the prodromal syndrome is more serious and can include fever, asthenia, nausea and vomiting, pharyngitis, and arthralgia. There is rapid involvement of mucosa, which can inhibit sound production, swallowing, and oral intake. Skin lesions are characterized by lack of symmetry and can involve mucous membranes, lips, and genitalia. It is important to distin-

guish this more serious form of disease because it can affect the lips, pharynx, larynx, esophagus, bronchial tree, kidney, and eyes, therefore leading to serious sequelae including dehydration, visceral organ damage from mucosal ulcerations, inflammatory renal lesions that could cause an acute glomerulonephritis-like syndrome, and ocular complications that can cause blindness.<sup>5,6</sup> Most mucocutaneous lesions tend to heal completely in 2 to 6 weeks, and fatal forms are exceptional (1 percent of cases in one series).<sup>5,7</sup>

Toxic epidermal necrolysis is the most serious form on this clinical spectrum, the hallmark of which is Nikolsky's sign (epidermal loss with lateral shearing force). Again there tends to be a more serious prodromal syndrome and then a burning or painful eruption, located symmetrically on the face and upper torso. This eruption rapidly extends to the entire body, although it predominates on the trunk and proximal limbs.<sup>6,8</sup> Such extensive skin involvement can lead to "acute skin failure," which can result in massive fluid loss, a hypercatabolic state, and bacterial colonization of skin resulting in systemic sepsis.<sup>9</sup> Mucous membrane involvement and ocular lesions can lead to serious above-mentioned sequelae. Up to 30 percent of cases can be fatal.<sup>6</sup>

### ***Treatment***

The progression of these diseases is difficult to predict, and treatment varies depending on clinical severity. Initial measures are termination of possible inciting medications, fluid replacement, symptomatic relief of itching and pain, and antibiotics for mouth and skin lesions with secondary infection. Whether to use systemic corticosteroids has remained the subject of controversy. They can decrease symptoms and retard the spread of lesions,<sup>2</sup> but they do not accelerate healing and might induce serious complications such as gastrointestinal bleeding and infection.<sup>10</sup> One measure that has reduced the recurrence rate of herpes-related erythema multiforme is oral acyclovir.<sup>2</sup> Because early intervention is crucial to preventing sequelae, prompt ophthalmic and dermatologic consultation should be sought in severe cases.

### ***Conclusion***

Erythema multiforme, although usually a self-limited disease, can be confused with the more severe disease states on the continuum. Because it can be

caused by many agents, a detailed history of the prodromal symptoms and extent of involvement is necessary to ascertain the severity of illness. Furthermore, a thorough physical examination, paying attention specifically to distribution of lesions and associated symptoms, is essential to determine what treatment regimen should be applied. Treatment measures are generally supportive, although the use of corticosteroids remains controversial. Prompt detection of oculocutaneous and visceral lesions should hasten referral to an ophthalmologist and dermatologist to prevent more serious sequelae from developing.

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