



Mildly pruritic palmar rash

After taking azithromycin and prednisone for lower respiratory symptoms, this patient developed a rash. The way it spread provided a diagnostic clue.

A **62-YEAR-OLD MAN** presented to the emergency department (ED) with a swollen, red, and painful right lower leg. He'd had bilateral lower leg swelling for 2 months, but the left leg became increasingly painful and red over the past 3 days. The patient also had a 3-day history of a diffuse rash that began on his right upper arm and spread to his left arm, both palms, both legs, and his back. It was mildly pruritic, but not painful.

The patient indicated that he had recently sought care from his primary care physician for lower respiratory symptoms. He had just completed a 5-day course of azithromycin and prednisone (50 mg/d for 5 days) the day before his ED visit.

A lower extremity venous ultrasound revealed that the patient had a deep vein thrombosis (DVT). Computed tomography (CT) imaging of the chest with contrast revealed pulmonary emboli. He was treated with enoxaparin and warfarin. We diagnosed the rash based on the patient's history and the appearance of the rash, which was comprised of blanching and erythematous macules with central clearing (**FIGURE 1**). (There were no blisters or mucosal involvement.)

- WHAT IS YOUR DIAGNOSIS?
- HOW WOULD YOU TREAT THIS PATIENT?

FIGURE 1

Erythematous macules with central clearing on palms



IMAGE COURTESY OF MORTEZA KHODAEI, MD, MPH

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➤ Herpes simplex virus is the most common infectious trigger for erythema multiforme.

**Diagnosis:
Erythema multiforme**

The clinical exam was consistent with the diagnosis of erythema multiforme (EM). A diagnosis of EM can usually be made based on the clinical exam alone.¹ Typical targetoid lesions have a round shape and 3 concentric zones: A central dusky area of epidermal necrosis that may involve bullae, a paler pink or edematous zone, and a peripheral erythematous ring.² Atypical lesions, such as raised papules, may also be seen.²

The skin lesions of EM usually appear symmetrically on the distal extremities and spread in a centripetal manner.¹ Palms, soles, and mucosa can be involved.¹ EM with mucosal involvement is called “erythema multiforme major,” and EM without mucosal

disease (as in our patient’s case) is called “erythema multiforme minor.”²

■ **EM is an acute, immune-mediated eruption** thought to be caused by a cell-mediated hypersensitivity to certain infections or drugs.² Ninety percent of cases are associated with an infection; herpes simplex virus (HSV) is the most common infectious agent.³ *Mycoplasma pneumoniae* is another culprit, especially in children. Medications are inciting factors about 10% of the time; nonsteroidal anti-inflammatory drugs, sulfonamides, antiepileptics, and antibiotics have been linked to EM eruptions.³

Interestingly, while azithromycin—the medication our patient had taken most recently—can cause EM, it has been mainly linked to cases of Stevens-Johnson syndrome

TABLE
Differential diagnosis of a non-vesicular palmar rash^{1,5-12}

Condition	Characteristics
Erythema multiforme	Typical targetoid lesions or atypical lesions with raised papules; distribution is symmetric and may involve soles, entire body, and, minimally, mucous membranes ¹
Stevens-Johnson syndrome (see FIGURE 2A)	Atypical targetoid lesions and confluent purpuric macules; severe mucosal erosions; <10% epidermal detachment ⁵⁻⁷
Toxic epidermal necrolysis	Atypical targetoid lesions; severe mucosal erosions; >30% epidermal detachment ⁵⁻⁷
Parvovirus B19 (see FIGURE 2B)	Erythematous, purpuric, reticulated, annular lesions; possible gloves-and-socks distribution, as well as trunk and face involvement; in children, a “slapped cheek” rash and fever ⁸
Coxsackievirus (hand, foot, and mouth disease) (see FIGURE 2C)	Macular, maculopapular, or vesicular rash of hands, feet, and mouth; may also present as widespread exanthema ⁹
Chronic liver disease	Painless, symmetric, non-pruritic, non-scaling erythema; usually most prominent on the thenar and hypothenar eminences of the palmar surface ¹⁰
Rickettsia (Rocky Mountain spotted fever)	Nonpruritic maculopapular rash that progresses to petechial lesions after several days; petechial lesions can coalesce to form ecchymosis; petechial lesions begin around wrists and ankles and eventually cover trunk and extremities, including palms and soles ⁵
Secondary syphilis (see FIGURE 2D)	Painless, non-pruritic, non-inflammatory, bilateral, reddish-brown, maculopapulonodular rash; distribution may involve soles, entire body, and mucous membranes ¹
Kawasaki disease (see FIGURE 2E)	Initially includes erythematous and edematous changes of the hands and feet; periungual desquamation of fingers and toes appear later in the convalescence phase; seen only in a pediatric population and associated with other symptoms of Kawasaki disease, such as fever, bilateral conjunctival injection, oral changes (cracked and erythematous lips and strawberry tongue), and cervical lymphadenopathy ¹²

FIGURE 2

Can you identify these conditions that may also present with a non-vesicular palmar rash?



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IMAGE COURTESY OF RICHARD P. USATINE, MD



IMAGE COURTESY OF PETER A. LIO, MD, AND ALISA MCGUIRE, MD



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IMAGE COURTESY OF RYAN P. JOHNSON, MD

- Clockwise from top left:**
- A. Stevens-Johnson syndrome
 - B. Parvovirus B19
 - C. Coxsackievirus (hand, foot, and mouth disease)
 - D. Secondary syphilis
 - E. Kawasaki disease.

CONTINUED

(SJS).⁴ So, while we suspect that azithromycin was the trigger in our patient's case, we can't be sure. It's also possible that *Mycoplasma pneumoniae* was the trigger for our patient's EM. However, *Mycoplasma pneumoniae* is more common in adolescents.

Differential includes life-threatening conditions like SJS

The differential diagnosis for a non-vesicular palmar rash is discussed in the TABLE.^{1,5-12} There is a wide spectrum of possible etiologies—from infectious and rheumatologic disorders to chronic liver disease. Histologic testing may be useful in differentiating EM from other diseases, but in most cases, it is not required to make a diagnosis.¹ Laboratory testing may reveal leukocytosis, an elevated erythrocyte sedimentation rate, and elevated liver function test results, but these are nonspecific.¹

It's important to differentiate EM from life-threatening conditions like SJS and toxic epidermal necrolysis (TEN).⁵ EM is characterized by typical and atypical targetoid lesions with minimal mucosal involvement.^{6,7} SJS is characterized by flat atypical targetoid lesions, confluent purpuric macules, severe mucosal erosions, and <10% epidermal detachment.^{6,7} TEN is characterized by severe mucosal erosions and >30% epidermal detachment.^{6,7}

Lesions resolve on their own, but topical steroids can provide relief

EM is a self-limiting disease; lesions resolve within about 2 weeks.³ Management begins by treating any suspected infection or discontinuing any suspected drugs.¹ In patients with co-existing or recurrent HSV infection, early treatment with an oral antiviral (such as acyclovir) may lessen the number and duration of lesions.^{1,6} In addition, oral antihistamines and topical steroids may be used to provide symp-

tomatic relief.^{1,6} Use of oral corticosteroids can be considered in severe mucosal disease, although such use is considered controversial due to a lack of evidence.^{1,6}

■ **Our patient** remained hospitalized for 4 days. As noted earlier, his DVT and pulmonary embolism were treated with enoxaparin and the patient was sent home with a prescription for warfarin. Regarding the EM, his rash and itching improved significantly during the hospitalization (without any specific treatment) and was mostly resolved at a follow-up visit 6 days after discharge. **JFP**

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➤ **It's important to differentiate erythema multiforme from Stevens-Johnson syndrome and toxic epidermal necrolysis.**

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