



# Generalized maculopapular rash and fever

Was this a case of the “great masquerader”? Or was it something else?

A 29-YEAR-OLD MAN was referred to the emergency department for fever and rash. Two months prior, he had noticed painful spots on his toes (FIGURE 1). Soon after, a rash of different morphology appeared on his chest and upper extremities. Associated symptoms included hair loss, generalized arthralgias, chills, trouble with balance, and photophobia. The patient denied genital lesions but reported 3 recent cold sores.

On exam, the patient was febrile (102 °F). Skin exam revealed a generalized maculopapular rash on the trunk, arms, and legs with scattered lesions on the palms (FIGURE 2). There were tender purpuric macules on the tips of his toes with areas of blanching. His hands had pink plaques on the dorsal fingers (FIGURE 3). Additionally, there was an

erythematous papular rash with scale on his cheeks and nasal bridge, patchy areas of hair loss, and a single oral ulcer.

A neurologic exam was notable for mildly unstable gait, an abnormal Babinski reflex on the left side, and a positive Romberg sign. Musculoskeletal exam revealed joint tenderness in his shoulders, elbows, and wrists. Lymphadenopathy was present bilaterally in the axilla.

Lab work was ordered, including a VDRL test and a treponemal antibodies test. Skin biopsies also were taken from lesions on his arm and chest.

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

**FIGURE 1**  
Painful lesions on toes



**FIGURE 2**  
Maculopapular rash on the trunk and arms



Alexandra Verdieck, MD;  
Eric Ardman, MD;  
Nicholas Defelice, MD  
Oregon Health and Science  
University, Portland

[verdieck@ohsu.edu](mailto:verdieck@ohsu.edu)

**DEPARTMENT EDITOR**

Richard P. Usatine, MD  
University of Texas Health,  
San Antonio

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### Diagnosis: Systemic lupus erythematosus

Our patient's fever and rash were highly suggestive of either systemic lupus erythematosus (SLE) or secondary syphilis (the "great masquerader").

In addition to the joint tenderness revealed during the musculoskeletal exam, our patient had several nonspecific lupus findings on skin exam: malar rash, discoid rash on hands, subacute vasculitis (generalized rash), alopecia, and an oral ulcer; he also had the specific finding of chilblains vasculitis of the toes. Lab work and pathology results made the diagnosis clear. Lab work revealed leukopenia, an antinuclear antibody (ANA) result of 1:2560 with speckled appearance, and positive anti-SM antibodies. A dipstick was negative for protein; VDRL and treponemal antibodies tests were also negative. Histopathology showed perivascular lymphohistiocytic vacuolar dermatitis with a differential of connective tissue disease, including lupus.

### Our patient met the criteria

SLE is a systemic autoimmune disease resulting in chronic inflammation in multiple organ systems; it commonly manifests with vague symptoms of fatigue, fever, and weight loss. The prevalence of SLE in the United States has been reported as high as 241 per 100,000

people.<sup>1</sup> Women are more likely to be affected, and the incidence is highest among Black people and lowest among Caucasians.<sup>1,2</sup> Risk factors include cigarette smoking and exposure to silica particulate air pollution.

The 2019 European League Against Rheumatism/American College of Rheumatology criteria for a diagnosis of SLE require that a patient have a positive ANA and some, but not all, additive lab, clinical, and organ-specific findings.<sup>3</sup> Findings that clinicians should look for include<sup>3,4</sup>

- elevated ANA ( $\geq 1:80$ )
- constitutional symptoms (fever)
- hematologic findings (leukopenia, thrombocytopenia, autoimmune hemolysis)
- neuropsychiatric findings (delirium, psychosis, seizure)
- mucocutaneous findings (alopecia, oral ulcers, others)
- serosal findings (effusion, acute pericarditis)
- musculoskeletal findings (joint involvement)
- renal findings (proteinuria)
- antiphospholipid antibodies
- decreased complement proteins
- SLE-specific antibodies.

■ **Dermatologic findings** occur in more than 70% of patients with SLE.<sup>5</sup> They can be nonspecific—eg, classic discoid rash, malar rash, alopecia, maculopapular rash (most commonly on sun-exposed areas, mimicking polymorphous light eruption)—or specific (eg, chilblains).<sup>5</sup>

### The differential for rash and fever is broad

■ **Syphilis** also can manifest with rash and fever. The rash of syphilis is nonpainful and affects the torso and face, with concentration on the palms and soles.<sup>6,7</sup> It manifests during syphilis's secondary stage, 6 to 8 weeks after an untreated infection. Fatigue, malaise, lymphadenopathy, mucosal lesions, ocular symptoms, and nephritis can occur.<sup>8,9</sup> The diagnosis is made through treponemal-specific antibody confirmation of a positive rapid plasma reagin test.<sup>9</sup> Neurosyphilis is diagnosed via lumbar puncture.<sup>9</sup>

FIGURE 3

### Plaques on the dorsal fingers



IMAGE COURTESY OF ERIC ARDMAN, MD

■ **Dermatomyositis** is a rare disorder of inflammation in both the skin and muscles. Symptoms include rash, muscle aches, and weakness. Lab abnormalities include elevated creatine kinase levels and ANA. Muscle biopsy confirms the diagnosis.

■ **Erythema multiforme** is an immunologic-mediated rash consisting of firm targetoid erythematous papules distributed symmetrically on the extremities, including palms/soles. It typically appears after a viral infection, immunization, or new medications (eg, antibiotics, nonsteroidal anti-inflammatory drugs, or phenothiazines) initiated 1 to 3 weeks prior to the appearance of the rash. History and appearance inform the diagnosis.

■ **Polymorphic light eruption** is a rash of variable appearance on sun-exposed areas that results from a sensitivity to sunlight after lack of exposure for a period of time. Symptoms include burning and itching.

## Treatment and outcome

Treat patients with SLE with hydroxychloroquine (200-400 mg/d) to suppress inflammation and with low-dose oral steroids such as prednisone (7.5 mg/d) for intermittent exacerbations. Higher steroid doses are sometimes needed for signs of organ inflammation. Patients with increased disease activity will require immunosuppressive therapy with disease-modifying antirheumatic drugs, such as methotrexate (7.5-25 mg/wk), mycopheno-

late (2-3 g/d), azathioprine (1.5-2.5 mg/kg/d), and biologic infusions.<sup>4</sup> Additionally, in 2021, the US Food and Drug Administration approved anifrolumab (Saphnelo) and voclosporin (Lupkynis) for the treatment of SLE.<sup>4</sup>

■ **Our patient** was admitted for further evaluation. A lumbar puncture was performed because of his balance issues; it showed an elevated protein level, but further work-up did not find an infectious or malignant source. Balance improved with hydration. The patient remained hospitalized for 9 days, during which his fever subsided. His pain improved after initiation of hydroxychloroquine 400 mg/d. Follow-up with Rheumatology was arranged for further care. **JFP**

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CONTINUED FROM PAGE 272

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