

Generalized rash and pruritus in a 58-year-old woman

Kristen M. Lutzkanin, M.D.,¹ Erin A. Davidowicz, B.S.,² Galen Foulke, M.D.,³ Sheva Khalafbeigi, M.D.,⁴ Alexandra Flamm, M.D.,³ and Faoud Ishmael, M.D.¹

ABSTRACT

Although allergists often evaluate rashes associated with allergic, IgE mediated etiologies, it is important to consider a wide range of differential diagnoses that includes inflammatory, infectious, and autoimmune etiologies. The case of a 58-year-old woman with a 1-year history of progressive pruritic rash that did not improve with topical creams and steroids is presented. The patient did not state any other symptoms, and a physical examination was notable for a widespread rash. After a detailed evaluation of the rash, a differential diagnosis was made, and results of a skin biopsy confirmed a specific diagnosis. Even in the context of a medical history of atopy, one must consider nonallergic causes of rash, including abnormal presentations of systemic conditions. It is important to determine the specific etiology of the rash because this will dictate treatment and prognosis and/or complications of the disease associated with the skin manifestations.

(Allergy Asthma Proc 39:468–471, 2018; doi: 10.2500/aap.2018.39.4181)

CHIEF CONCERN

The patient complained of itchy rash.

HISTORY OF PRESENT ILLNESS

A 58-year-old woman presented with a 1-year history of an erythematous, pruritic rash. It started on her hips and spread to her arms, scalp, face, chest, back, and, most recently, her bilateral thighs. She reported prominent scalp itch. She did not have other physical concerns. The patient did not use any new laundry detergents, perfumes, cosmetics, nail polish, or hair products, and did not have variations in her diet.

MEDICAL HISTORY

The patient's medical history was remarkable for asthma, allergic rhinitis, Grave disease, celiac disease, and atopic dermatitis (AD). There was a family history of AD and multiple sclerosis.

PHYSICAL EXAMINATION

The patient's vital signs were normal. She exhibited pink macules on her face in a malar distribution and diffuse erythema over her chest in a V-neck distribution as well as the upper back, shoulders, and neck. There were pink papules on the bilateral hips and forearms, and crusting, scaly red plaques on the bilateral anterior thighs. She had scaly, violaceous plaques over the knuckles, with pitting and/or ridging of fingernails (Fig. 1). Muscle strength and the remainder of her examination was normal.

LABORATORY AND OTHER DIAGNOSTIC FINDINGS

The patient had a normal complete blood cell count, and comprehensive metabolic panel was normal. Results of antinuclear antibody, anti-histone antibody, and anti-Mi-2 antibody were positive (Table 1).

CLINICAL COURSE

The rash persisted over the past year and did not improve, despite multiple courses of prednisone and trials of high-potency topical corticosteroids. She was seen by an allergist, who thought that the rash could be secondary to medication, but symptoms did not improve after stopping the medication. She was treated with topical permethrin and oral ivermectin for the possibility of scabies and a parasitic infection, but there was no symptomatic improvement.

QUESTION 1

- What is the differential diagnosis?
a. AD

From the ¹Section of Allergy and Immunology, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania, ²Penn State College of Medicine, Hershey, Pennsylvania, ³Department of Dermatology, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania, and ⁴Department of Dermatology and Pathology, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania

No external funding sources reported

The authors have no conflicts of interest to declare pertaining to this article

Address correspondence to Kristen M. Lutzkanin, M.D., Section of Allergy and Immunology, Penn State Milton S. Hershey Medical Center, 500 University Drive, P.O. Box 850, Mail Code H041, Hershey, PA 17033

E-mail address: klutzkanin@pennstatehealth.psu.edu

Copyright © 2018, OceanSide Publications, Inc., U.S.A.



Figure 1. Photograph of the patient's hand, demonstrating rash over the knuckles and periungual and nail bed changes.

- b. Contact dermatitis (CD)
- c. Subacute cutaneous lupus erythematosus (SCLE)
- d. Polymorphous light eruption (PLE)
- e. Dermatomyositis (DM)

QUESTION 2

What diagnostic studies should be performed?

A skin biopsy is the next logical step. A shave biopsy of the right hand and a punch biopsy of the left lateral hip were performed. Results of the shave biopsy demonstrated hyperkeratosis and mild epidermal atrophy. An interface dermatitis was noted, with scattered dyskeratotic keratinocytes seen. A mild lymphocytic inflammatory infiltrate was noted in the superficial dermis with dermal mucin deposition (Fig. 2). She was scheduled for a follow-up appointment in the rheumatologic dermatology specialty clinic, with additional workup to rule out comorbid medical conditions.

DISCUSSION

Pruritic rashes are very common and have a broad differential diagnosis, including diseases with allergic, genetic, infectious, and autoimmune etiologies. Although rashes are commonly associated with allergic etiologies, there may be more complex etiologies with severe complications that require prompt diagnosis and more aggressive treatments.¹ Therefore, in a patient with widespread skin findings and a significant history of autoimmune conditions, the provider must have a high suspicion for uncommon variants of more complex conditions.

AD and CD are both characterized by intense pruritus. Acute AD is associated with erythematous pap-

Table 1 Laboratory results

	Results	Reference Range
White blood cell count, k/ μ L	5.52	4–10.4
Hemoglobin level, g/dL	12.8	11.7–15
Hematocrit, %	38.2	35–44
Platelets, k/ μ L	301	150–350
Absolute neutrophils, k/ μ L	2.73	2–7.7
Absolute lymphocytes, k/ μ L	2.14	1–3.4
Absolute eosinophils, k/ μ L	0.10	0–0.5
ALT level, U/L	9	0–33
AST level, U/L	17	0–32
Alkaline phosphatase level, U/L	67	35–115
Total bilirubin level, mg/dL	0.2	0–1.2
CPK level, U/L	59	26–192
ANA	1:640 speckled H	<1:40
Anti-double-stranded DNA, IU/mL	10.29	<30
Anti-Smith, U/mL	5.7	<20
Anti-RNP, U/mL	5.26	<20
Anti-SSA, U/mL	3.33	<20
Anti-SSB, U/mL	3.33	<20
Anti-centromere B, U/mL	12.15	<20
Anti-SCL70, U/mL	4.58	<20
Anti-histone, U/mL	2.17 H	<1
Anti-JO1, U/mL	3.86	<20
Anti-SRP	None detected	None detected
Anti-Mi-2	None detected	None detected
CRP level, mg/dL	0.13	<0.5

ALT = Alanine aminotransferase; AST = aspartate aminotransferase; CPK = creatine phosphokinase; ANA = antinuclear antibody; RNP = ribonucleoprotein; SSA = Sjögren's-syndrome-related antigen A; SSB = Anti-Sjögren's-syndrome-related antigen B; SRP = signal recognition particle; CRP = C-reactive protein.

ules, plaques, and vesicles, usually localized to flexural surfaces in adults, whereas chronic AD is dry and/or scaly patches often with excoriation or lichenification.² CD, which is typically localized, can also be acute or chronic, with the acute phase characterized by erythematous papules and/or plaques. Chronic CD presents with dry, scaly, thickened skin. Symptoms resolve with topical steroids and, in the case of CD, with



Figure 2. Shave biopsy of the right hand, showing an interface dermatitis with scattered dyskeratotic keratinocytes.

removal of the offending agent. Scalp itch is not pronounced in AD or CD as it is in other skin conditions unless the allergen is being applied directly to the scalp. Due to the widespread rash and lack of response to topical and oral steroids, AD and CD were excluded.³

SCLE most commonly presents as the “psoriasiform/papulosquamous” and the “annular-polycyclic” variant. The primary lesion is usually an erythematous papule or plaque covered with fine scales that either expand or merge into retiform arrays of papulosquamous lesions or develop central clearing and produce annular lesions that merge into polycyclic arrays. These lesions normally occur in sun-exposed areas and are associated with significant light sensitivity, musculoskeletal symptoms, and systemic symptoms.⁴ SCLE typically responds to systemic steroids, which makes this a less likely cause of rash in our patient.

PLE is characterized by pruritic skin lesions, including papules, plaques, vesicles, and targetoid macules, that occur on sun-exposed areas during spring or early summer. These lesions occur hours to days after exposure to sunlight and resolve after a few days if sunlight is avoided. These lesions are often indistinguishable from cutaneous lupus, and the antinuclear antibody level can be elevated in both PLE and cutaneous lupus. Lesions are prevented by avoiding sun exposure, and lesions are treated with topical oral steroids, depending on severity.⁵ The distribution of the patient’s rash and the elevated antinuclear antibody level could be consistent with PLE, but the persistent nature of the rash and the lack of improvement with steroids make the diagnosis less likely.

DM is an idiopathic inflammatory myopathy (IIM). In addition to the features of proximal muscle weakness and muscle inflammation, DM also has specific cutaneous manifestations associated with the disease: Gottron’s papules (pink to violaceous papules that symmetrically involve the dorsal aspects of the metacarpophalangeal and interphalangeal joints); Gottron’s sign (pink to violaceous macules, patches, or papules

that involve extensor surfaces of other joints); heliotrope rash; facial erythema; generalized erythroderma; photograph-distributed poikiloderma (including the V-neck and shawl sign in photo-exposed areas to upper chest and/or upper back); Holster sign (poikiloderma on the lateral aspects of the thighs); and periungual abnormalities, including dilated nail bed capillary loops, periungual erythema, and ragged cuticles (Samitz sign).⁶

A less well-recognized subtype of DM found in ~20% of cases,⁷ amyopathic dermatomyositis (ADM) is associated with the characteristic skin manifestations of DM, without skeletal muscle weakness or diagnostic findings of muscular inflammation.⁸ However, skin findings of DM may precede the onset of muscle weakness,⁹ which indicates that a patient with solitary cutaneous findings may be early on in the disease process of classic DM.⁶

Historically, the diagnosis of DM was made by using the Bohan and Peter criteria,^{10,11} which relied on the presence of muscular involvement on examination, laboratory and electromyography studies, and typical muscle biopsy findings, including “necrosis, phagocytosis, regeneration, and inflammation.”^{10,11} Dermatologic features of DM were also part of the criteria.^{10,11} Newer criteria, proposed by Sontheimer¹² for ADM dropped the requirement of muscle biopsy, abnormal laboratories, and electromyographies, and, instead, relied on the presence of classic skin manifestations of DM for >6 months in the absence of muscle involvement (on examination or laboratory evaluation), with a skin biopsy result consistent with DM.¹²

Of patients with classic DM, 95% will have an elevation in serum aldolase and creatine kinase (CK), which indicates muscular involvement.⁶ The CK value may be elevated by 50 times the normal level in patients with DM but is a nonspecific enzyme marker.⁹ Other studies that can be performed to demonstrate muscular inflammation include lactate dehydrogenase, aspartate aminotransferase, alanine aminotransferase.⁶ Antihistone antibodies may also be present in inflammatory myopathies.¹³

Autoantibodies are important for confirming the diagnosis of DM and can be identified in >80% of patients with autoimmune myositis, but they are not required for diagnosis. Myositis-specific antibodies, including anti-aminoacyl-tRNA (transfer RNA) synthetase, anti-Mi-2, anti-SRP, and several novel antibodies, including anti-TIF1-gamma, have a specificity of greater than 90% for autoimmune myositis when present.¹⁴ Further confirmatory testing can include muscle biopsy and skin biopsy. If there is skin involvement characteristic of DM, associated with other typical clinical features of DM, then a muscle biopsy can be avoided. Skin biopsy would reveal atrophy of epidermis, associated with vacuoles in the basal keratinocyte

layer and with perivascular and lichenoid interface lymphocytic infiltrate.⁷

In addition to the typical cutaneous and muscular involvement, DM is often associated with involvement with other organs. Interstitial lung disease (ILD) is often associated with the IIMs and is seen in ~5 to 40% of patients with DM.⁶ The most common patterns of myositis-associated ILD histology in lung biopsy include nonspecific interstitial pneumonia, general interstitial pneumonia, organizing pneumonia, diffuse alveolar damage, and lymphocytic interstitial pneumonia. The presence of ILD indicates a worse prognosis and requirement of more aggressive therapy for the patient.¹⁵ Patients with DM have an ~25% chance of developing a malignancy, particularly adenocarcinoma of the breast, lung, gastrointestinal tract, and ovaries.⁶ The increased risk for malignancy lasts for 3 years after initial onset of the symptoms; the risk returns to baseline by year 5.¹⁶

Treatment and management of DM vary with the specific presentation of the patient. Immunosuppressants are the criterion standard for treating dermatomyositis, and systemic prednisone is the most commonly used.⁶ Muscle inflammation is much more responsive to prednisone than the skin manifestations.⁶ If symptoms do not resolve or if the patient relapses, then a second-line immunosuppressant can be added, such as methotrexate or intravenous immunoglobulin.⁹ In patients with ADM that is refractory to prednisone, the medical literature demonstrates improvement with topical corticosteroids or tacrolimus, and avoidance of sunlight, but most cases require systemic therapy.⁶ The prognosis of DM is variable, depending on the timing of the diagnosis and the presence of extramuscular manifestations, including ILD and malignancy.⁶ Severe forms of ILD can worsen the prognosis, *e.g.*, rapidly progressive ILD that can be associated with ADM.¹⁷

FINAL DIAGNOSIS

ADM.

REFERENCES

1. Ely JW, Seabury Stone M. The generalized rash: part I. Differential diagnosis. *Am Fam Physician*. 2010; 81:726–734.
2. Watson W, Kapur S. Atopic dermatitis. *Allergy Asthma Clin Immunol*. 2011; 7(Suppl 1):S4.
3. Nelson JL, Mowad CM. Allergic contact dermatitis: patch testing beyond the TRUE test. *J Clin Aesthet Dermatol*. 2010; 3:36–41.
4. Fabbri P, Cardinali C, Giomi B, Caproni M. Cutaneous lupus erythematosus: diagnosis and management. *Am J Clin Dermatol*. 2003; 4:449–465.
5. Gruber-Wackernagel A, Byrne SN, Wolf P. Polymorphous light eruption: clinic aspects and pathogenesis. *Dermatol Clin*. 2014; 32:315–334, viii.
6. Strowd LC, Jorizzo JL. Review of dermatomyositis: establishing the diagnosis and treatment algorithm. *J Dermatolog Treat*. 2013; 24:418–421.
7. Gazeley DJ, Cronin ME. Diagnosis and treatment of the idiopathic inflammatory myopathies. *Ther Adv Musculoskelet Dis*. 2011; 3:315–324.
8. Dalakas MC, Hohlfield R. Polymyositis and dermatomyositis. *Lancet*. 2003; 362:971–982.
9. Amato AA, Barohn RJ. Evaluation and treatment of inflammatory myopathies. *J Neurol Neurosurg Psychiatry*. 2009; 80:1060–1068.
10. Bohan A, Peter JB. Polymyositis and dermatomyositis (first of two parts). *N Engl J Med*. 1975; 292:344–347.
11. Bohan A, Peter JB. Polymyositis and dermatomyositis (second of two parts). *N Engl J Med*. 1975; 292:403–407.
12. Euwer RL, Sontheimer RD. Amyopathic dermatomyositis (dermatomyositis sine myositis). Presentation of six new cases and review of the literature. *J Am Acad Dermatol*. 1991; 24:959–966.
13. Kubo M, Ihn H, Yazawa N, Sato S, Kikuchi K, Tamaki K. Prevalence and antigen specificity of anti-histone antibodies in patients with polymyositis/dermatomyositis. *J Invest Dermatol*. 1999; 112:711–715.
14. Ghirardello A, Borella E, Beggio M, Franceschini F, Fredi M, Doria A. Myositis autoantibodies and clinical phenotypes. *Auto Immun Highlights*. 2014; 5:69–75.
15. Zhang L, Wu G, Gao D, et al. Factors associated with interstitial lung disease in patients with polymyositis and dermatomyositis: a systematic review and meta-analysis. *PLoS One*. 2016; 11:e0155381.
16. Oldroyd A, Lilleker J, Chinoy H. Idiopathic inflammatory myopathies - a guide to subtypes, diagnostic approach and treatment. *Clin Med (Lond)*. 2017; 17:322–328.
17. Hirakata M, Nagai S. Interstitial lung disease in polymyositis and dermatomyositis. *Curr Opin Rheumatol*. 2000; 12:501–508. □

Copyright of Allergy & Asthma Proceedings is the property of OceanSide Publications Inc. and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.