ONLINE EXCLUSIVE

Worsening skin lesions but no diagnosis

A diagnosis was arrived at by doing something that the patient's other doctors hadn't: perform a biopsy.

Julia Lubsen, MD
Department of Family Medicine and Community Health, University of Wisconsin School of Medicine and Public Health, Madison

julia.lubsen@fammed.wisc.edu

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

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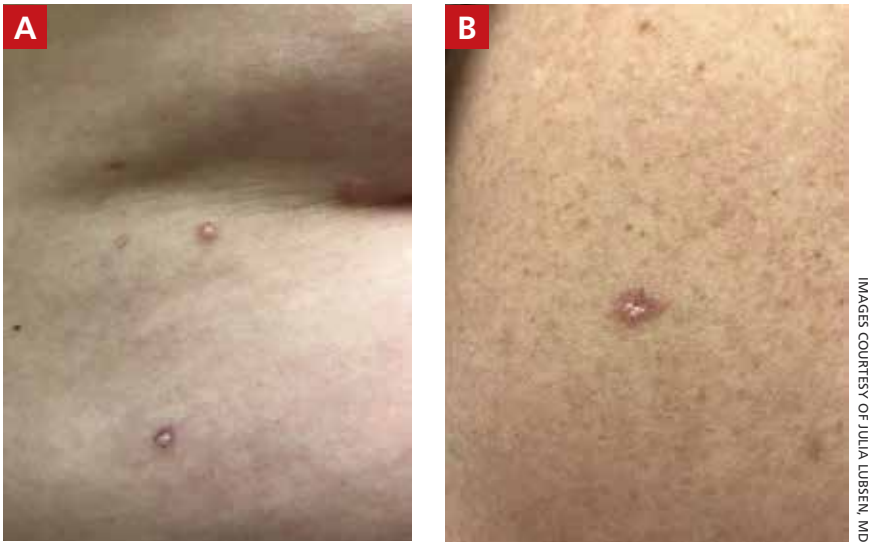
A 50-YEAR-OLD WOMAN presented to her family physician for a urinary tract infection (UTI) and an itchy rash. She said the rash had developed 2 years earlier and had gotten worse, with additional lesions emerging on her skin as time went on. She noted that other physicians had evaluated the rash but provided no clear diagnosis and had done no testing.

A physical exam revealed scattered erythematous papules with white centers on the patient's trunk, arms, and legs (**FIGURE 1**). The patient's medical history was significant for asthma, obstructive sleep apnea, obesity, gastroesophageal reflux disease, urinary incontinence, and depression. Her medications included montelukast, inhaled fluticasone, albuterol, tolterodine, omeprazole, and fluoxetine.

The patient was prescribed nitrofurantoin, 100 mg twice daily for 5 days, to treat her UTI, and a punch biopsy was performed on one of the patient's lesions to determine the cause of the rash.

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

FIGURE 1
Scattered erythematous papules with white centers on the lower back (A) and left upper arm (B)



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Diagnosis: Atrophic papulosis

Pathology suggested a diagnosis of atrophic papulosis. A consultation with a dermatologist and additional biopsies confirmed the diagnosis. The biopsies showed wedge-shaped areas of superficial dermal sclerosis with thinning of the overlying epidermis. The superficial dermal vessels contained scattered, small thrombi at the periphery of the areas of sclerosis.

Atrophic papulosis (also known as *Degos disease* or *Kölmeier-Degos disease*) is a vasculopathy characterized by thrombotic occlusion of small arteries.[1] Although rare—with fewer than 200 published case reports in the literature—it is likely underdiagnosed.[1] Atrophic papulosis can be distinguished by hallmark skin findings, including 0.5- to 1-cm papular skin lesions with central porcelain-white atrophy and an erythematous, telangiectatic rim.[1] It usually manifests between ages 20 to 50 but can occur in infants and children.[1] The etiology is unknown, but case evidence suggests the condition is sometimes familial.[1,2]

Easy to confuse with common conditions

Clinical presentation of atrophic papulosis can vary, but evaluation should rule out systemic lupus erythematosus and other connective tissue diseases.[1] In addition, the lesions can easily be confused with other common conditions such as molluscum contagiosum or insect bites.

The hallmark finding of molluscum contagiosum is raised papules with central umbilication, whereas atrophic papulosis lesions are characterized by white centers. While insect bites typically disappear within weeks, atrophic papulosis lesions persist for years or are even lifelong.[1]

Is it benign or malignant?

Benign atrophic papulosis is limited to the skin.[1] The probability of a patient having benign atrophic papulosis is about 70% at the onset of skin lesions and 97% after 7 years without other symptoms.[2]

Malignant atrophic papulosis—although less common—is systemic and life-threatening. About 30% of patients with atrophic papulosis develop lesions manifesting both on the skin and in internal organs.[1,2] Systemic involvement can develop at any time, sometimes years after the appearance of skin lesions, but the risk declines over time.[2] In a case series, systemic signs were shown to develop, on average, 1 year after skin lesions.[2] Some evidence suggests a mortality rate of 50% within 2 to 3 years of the onset of systemic involvement, making regular follow-up necessary.[1]

Patients with malignant atrophic papulosis may have systemic involvement in multiple organ systems. Gastrointestinal (GI) involvement can cause bowel perforation. Central nervous system (CNS) involvement may put the patient at risk for stroke, intracranial bleeding, meningitis, and encephalitis.[1,3] There can also be cardiopulmonary involvement that causes pleuritis and pericarditis.[1] Ocular involvement can affect the eyelids, conjunctiva, retina, sclera, and choroid plexus.[1] Renal involvement has been noted in a few cases.[2]

In a prospective, single-center cohort study of 39 patients with atrophic papulosis, systemic involvement (malignant atrophic papulosis) was reported in 29% (n = 11) of the patients.[2] In these patients, involved organ systems included the GI tract (73%; n = 8), CNS (64%; n = 7), eye (18%; n = 2), heart (18%; n = 2), and lungs (9%; n = 1); 64% (n = 7) had multiorgan involvement. Mortality was reported in 73% of the patients with systemic disease.

Ongoing testing is required

For a patient presenting with atrophic papulosis, initial and follow-up visits should include evaluation for systemic manifestations through a full skin examination, fecal occult blood test, and ocular fundus examination.[1,2] If the patient shows any symptoms that suggest systemic involvement, further testing is advised, including evaluation of renal function, colonoscopy, endoscopy, magnetic resonance imaging of the brain, an echocardiogram, and chest computed tomography.

Because internal organ involvement in malignant atrophic papulosis can develop within years of (benign) cutaneous manifestations, regular follow-up is recommended.[1] Research suggests evaluation of patients with benign atrophic papulosis every 6 months for

the first 7 years after disease onset and then yearly between 7 and 10 years after onset.[2]

Treatment options are limited

Antiplatelet agents (aspirin, pentoxifylline, dipyridamole, and ticlodipine) and anticoagulants (heparin) have led to partial regression of skin lesions in case reports.[1] Some lesions seem to disappear after treatment, but due to limited evidence, it is difficult to determine whether treatment leads to a reduction of future lesions.

When it comes to malignant atrophic papulosis, there is no uniformly effective treatment. Antiplatelet agents and anticoagulants are often used as initial treatment, but efficacy has not been clearly demonstrated. In case reports, eculizumab and treprostinil have shown effectiveness in treating CNS involvement, but there are no uniform dosage recommendations.[3,4]

In this case, the patient had mild GI symptoms. A colonoscopy showed evidence of microscopic colitis, but there was no evidence of atrophic papulosis in the GI tract.

Additional laboratory work-up was ordered to evaluate for signs of organ involvement and to rule out any associated connective tissue disease or hypercoagulable state. Her results showed a mildly elevated erythrocyte sedimentation rate (29 mm/h) and a positive antinuclear antibodies assay (1:640, speckled pattern). She was referred to a rheumatologist, who found no evidence of a connective tissue disorder. A complete blood count, comprehensive metabolic panel, urinalysis, and hypercoagulability work-up were all within normal limits. A complete eye exam was also normal.

The patient was started on aspirin 81 mg/d. Because she continued to develop new lesions, her dermatologist added pentoxifylline extended release and gradually increased the dose to 400 mg in the morning and 800 mg in the evening. About 4 years after onset of the rash, the patient showed no signs of systemic involvement, but her skin lesions were still present. JFP

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