

Clinical Manifestation of Degos Disease: Painful Penile Ulcers

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PRACTICE POINTS

- Papules with atrophic white centers and erythematous telangiectatic rims are the characteristic skin lesions found in Degos disease.
- A painful penile ulceration also may occur in Degos disease, though it is uncommon.
- The histopathology of skin lesions changes as the lesions evolve. Early lesions may resemble connective tissue disease. Late lesions show the classic pathology of wedge-shaped dermal sclerosis.

To the Editor:

A 56-year-old man was referred to our Grand Rounds by another dermatologist in our health system for evaluation of a red scaly rash on the trunk that had been present for more than a year. More recently, over the course of approximately 9 months he experienced recurrent painful penile ulcers that lasted for approximately 4 weeks and then self-resolved. He had a medical history of central retinal vein occlusion, primary hyperparathyroidism, and nonspecific colitis. A family history was notable for lung cancer in the patient's father and myelodysplastic syndrome and breast cancer in his mother; however, there was no family history of a similar rash. A bacterial culture of the penile ulcer was negative. Testing for antibodies against HIV and herpes simplex virus (HSV) types 1 and 2 was negative. Results of a serum VDRL test were nonreactive, which ruled out syphilis. The patient was treated by the referring dermatologist with azithromycin for possible chancroid without relief.

The patient was being followed by the referring dermatologist who initially was concerned for Degos disease

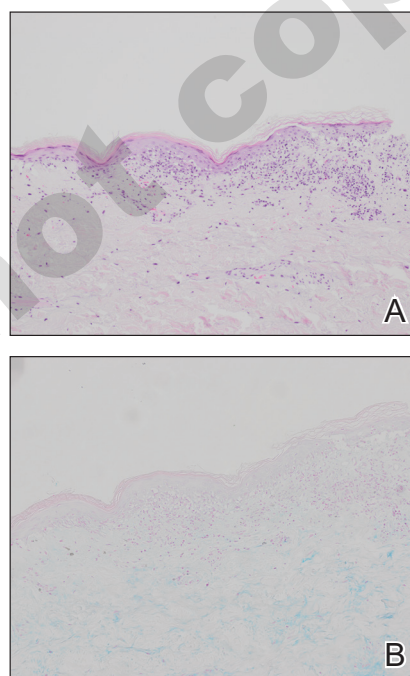


FIGURE 1. A, Initial biopsy of the back showed vacuolar interface dermatitis and a sparse superficial perivascular lymphocytic infiltrate (H&E, original magnification $\times 100$). B, Alcian blue stain highlighted increased dermal mucin (original magnification $\times 100$). Photographs courtesy of Jennifer Leininger, MD (Cedar Park, Texas).

based on clinical examination findings, prompting biopsy of a lesion on the back, which revealed vacuolar interface dermatitis, a sparse superficial perivascular lymphocytic infiltrate, and increased mucin—all highly suspicious for connective tissue disease (Figure 1). An antinuclear antibody test was positive, with a titer of 1:640. The patient was started on prednisone and referred to rheumatology;

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however, further evaluation by rheumatology for an autoimmune process—including anticardiolipin antibodies—was unremarkable. A few months prior to the current presentation, he also had mildly elevated liver function test results. A colonoscopy was performed, and a biopsy revealed nonspecific colitis. A biopsy of the penile ulcer also was nonspecific, showing only ulceration and acute and chronic inflammation. No epidermal interface change was seen. Results from a Grocott-Gomori methenamine-silver stain, *Treponema pallidum* immunostain, and HSV polymerase chain reaction were negative for fungal organisms, spirochetes, and HSV, respectively. The differential diagnosis included trauma, aphthous ulceration, and Behçet disease. Behçet disease was suspected by the referring dermatologist, and the patient was treated with colchicine, prednisone, pimecrolimus cream, and topical lidocaine; however, the lesions persisted, and he was subsequently referred to our Grand Rounds for further evaluation.

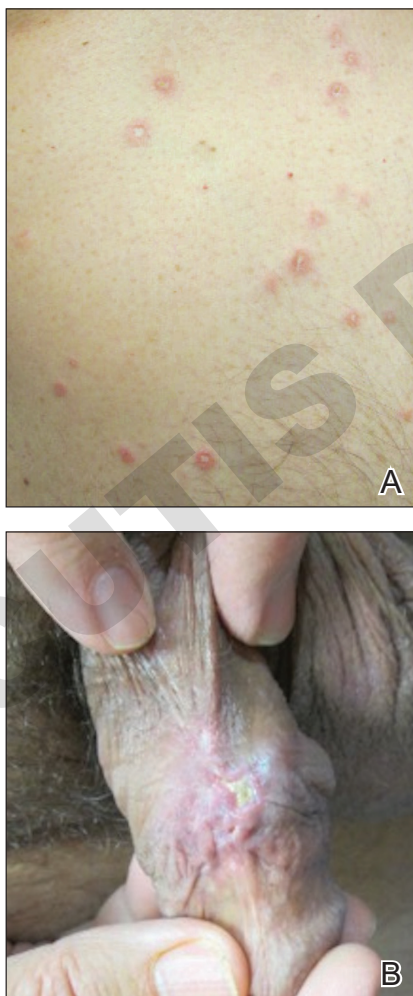


FIGURE 2. Degos disease. A, Papules with white atrophic centers and erythematous rims on the anterior trunk. B, An ulceration on the penile shaft.

At the current presentation, physical examination revealed several small papules with white atrophic centers and erythematous rims on the trunk and extremities (Figure 2A). An ulceration was noted on the penile shaft (Figure 2B). Further evaluation for Behçet disease, including testing for pathergy and HLA-B51, was negative. Degos disease was strongly suspected clinically, and a repeat biopsy was performed of a lesion on the abdomen, which revealed central epidermal necrosis, atrophy, and parakeratosis with an underlying wedge-shaped dermal infarct surrounded by multiple small occluded dermal vessels, perivascular inflammation, and dermal edema (Figure 3). Direct immunofluorescence was performed using antibodies against IgG, IgA, IgM, fibrinogen, albumin, and C3, which was negative. These findings from direct immunofluorescence and histopathology as well as the clinical presentation were considered compatible with Degos disease. The patient was started on aspirin and pentoxifylline. Pentoxifylline 400 mg twice daily appeared to lessen some of the pain. Pain management specialists started the patient on gabapentin.

Approximately 4 months after the Grand Rounds evaluation, during which time he continued treatment with pentoxifylline, he was admitted to the hospital for intractable nausea and vomiting. His condition acutely declined due to bowel perforation, and he was started on eculizumab 1200 mg every 14 days. Because of an increased risk for meningococcal meningitis while on this

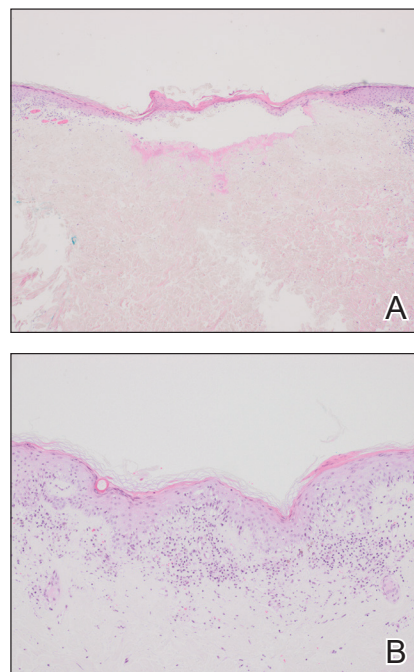


FIGURE 3. A, A biopsy of a lesion on the abdomen showed central epidermal necrosis and parakeratosis with an underlying wedge-shaped dermal infarct (H&E, original magnification $\times 40$). B, The infarct was surrounded by small occluded dermal vessels (H&E, original magnification $\times 100$).

medication, he also was given erythromycin 500 mg twice daily prophylactically. He was being followed by hematology for the vasculopathy, and they were planning to monitor for any disease changes with computed tomography of the chest, abdomen, and pelvis every 3 months, as well as echocardiogram every 6 months for any development of pericardial or pleural fibrosis. Approximately 1 month later, the patient was admitted to the hospital again but died after 1 week from gastrointestinal complications (approximately 22 months after the onset of the rash).

Degos disease (atrophic papulosis) is a rare small vessel vasculopathy of unknown etiology, but complement-mediated endothelial injury plays a role.^{1,2} It typically occurs in the fourth decade of life, with a slight female predominance.^{3,4} The skin lesions are characteristic and described as 5- to 10-mm papules with atrophic white centers and erythematous telangiectatic rims, most commonly on the upper body and typically sparing the head, palms, and soles.¹ Penile ulceration is an uncommon cutaneous feature, with only a few cases reported in the literature.^{5,6} Approximately one-third of patients will have only skin lesions, but two-thirds will develop systemic involvement 1 to 2 years after onset, with the gastrointestinal tract and central nervous system most commonly involved. For those with systemic involvement, the 5-year survival rate is approximately 55%, and the most common causes of death are bowel perforation, peritonitis, and stroke.^{3,4} Because some patients appear to never develop systemic complications, Theodoridis et al⁴ proposed that the disease be classified as either malignant atrophic papulosis or benign atrophic papulosis to indicate the malignant systemic form and the benign cutaneous form, respectively.

The histopathology of Degos disease changes as the lesions evolve.⁷ Early lesions show a superficial and deep perivascular and periadnexal lymphocytic infiltrate, possible interface dermatitis, and dermal mucin resembling lupus. The more fully developed lesions show a greater degree of inflammation and interface change as well as lymphocytic vasculitis. This stage also may have epidermal atrophy and early papillary dermal sclerosis resembling lichen sclerosis. The late-stage lesions, clinically observed as papules with atrophic white centers and surrounding erythema, show the classic pathology of wedge-shaped dermal sclerosis and central epidermal atrophy with surrounding hyperkeratosis. Interface dermatitis and dermal mucin can be seen in all stages, though mucin is diminished in the later stage.

Effective treatment options are limited; however, anti-thrombotics or compounds that facilitate blood perfusion, such as aspirin or pentoxifylline, initially can be used.¹ Eculizumab, a humanized monoclonal antibody that prevents the cleavage of C5, has been used for salvage

therapy,⁸ as in our case. Treprostinil, a prostacyclin analog that causes arterial vasodilation and inhibition of platelet aggregation, has been reported to improve bowel and cutaneous lesions, functional status, and neurologic symptoms.⁹

Our case highlights important features of Degos disease. First, it is important for both the clinician and the pathologist to recognize that the histopathology of Degos disease changes as the lesions evolve. In our case, although the lesions were characteristic of Degos disease clinically, the initial biopsy was suspicious for connective tissue disease, which led to an autoimmune evaluation that ultimately was unremarkable. Recognizing that early lesions of Degos disease can resemble connective tissue disease histologically could have prevented this delay in diagnosis. However, Degos disease has been reported in association with autoimmune diseases.¹⁰ Second, although penile ulceration is uncommon, it can be a prominent cutaneous manifestation of the disease. Finally, eculizumab and treprostinil are therapeutic options that have shown some efficacy in improving symptoms and cutaneous lesions.^{8,9}

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