

Is Degos' disease a clinical and histological end point rather than a specific disease?

Whitney A. High, MD, Jennifer Aranda, MD, Samir B. Patel, MD,
Clay J. Cockerell, MD, and Melissa I. Costner, MD
Dallas, Texas

Degos' disease is described as a rare disorder, with approximately 100 cases detailed in the literature. Nearly all are characterized by the near "pathognomonic" appearance of porcelain-white, atrophic papules with peripheral erythema and telangiectases. Many Degos' disease variants have been described including benign cutaneous Degos' disease, familial Degos' disease, atrophie blanche with Degos'-like features, and connective tissue diseases with similar findings. The course, prognosis, and treatment have substantially varied. We present four patients: the first carries a diagnosis compatible with classic Degos' disease, the second and third demonstrate cutaneous and histological findings of Degos' disease but laboratory evidence suggestive of lupus erythematosus, while the fourth has dermatomyositis with Degos'-like lesions. Because of broad overlap in clinical and histological findings, we contend that Degos' disease may not be a specific entity, but rather, may represent a common end point to a variety of vascular insults, many of which have not been fully elucidated. (*J Am Acad Dermatol* 2004;50:895-9.)

Degos' disease was first described in 1941 by Kohlmeier, and independently, by Degos in 1942.^{1,2} Over 100 cases have been detailed in the literature, nearly all characterized by the "pathognomonic" appearance of porcelain-white, atrophic papules with peripheral erythema and telangiectases. A vaso-occlusive process of unknown etiology, Degos' disease can be fatal due to involvement of the gastrointestinal tract or central nervous system.

Many Degos' disease variants have been detailed, including benign cutaneous Degos' disease, familial Degos' disease, atrophie blanche with Degos'-like features, systemic lupus erythematosus with Degos'-like lesions, dermatomyositis with Degos'-like lesions, and other connective tissue diseases with similar findings.³⁻¹² The course, prognosis, and treatment in these cases has substantially varied.

We present 4 patients: the first carries a diagnosis compatible with classic Degos' disease, the second and third demonstrate cutaneous and histological

findings of Degos' disease but laboratory evidence reminiscent of lupus erythematosus, while the fourth has dermatomyositis with Degos'-like lesions. Because of broad overlap in clinical and histological findings, we contend that Degos' disease may not exist as a specific entity, but rather, represents a common end point to a variety of vascular insults, many of which have not been fully elucidated.

CASE REPORTS

Case 1

A 56-year-old woman was referred for a papular eruption of 6 years duration. Lesions would progress from fleshy papules to atrophic scars with rosy erythema and telangiectases (Fig 1). They began on the extremities and progressed to involve the trunk.

Prednisone and hydroxychloroquine had been ineffective. Past medical history was significant for a perforated gastric ulcer. Family history was noncontributory. Anti-nuclear antibody (ANA), extractable nuclear antigen (ENA), complement, and coagulation studies including lupus anticoagulant, antiphospholipid antibodies, diluted viper venom testing, prothrombin time, activated partial thromboplastin time, protein C/S, factor V Leiden, and anti-thrombin III were unremarkable. A working diagnosis of atypical discoid lupus was assigned based on biopsy results from an outside institution.

She was treated with combination antimalarials and dapsone without improvement. A repeat biopsy was performed, which revealed a wedge-shaped zone of necrosis, scattered necrotic keratinocytes,

From the Department of Dermatology, The University of Texas Southwestern Medical Center at Dallas.

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Reprint requests: Melissa Costner, MD, Department of Dermatology, UTSW Medical Center, 5323 Harry Hines Blvd F4.100, Dallas, TX 75390-9069. E-mail: melissa.costner@utsouthwestern.edu.

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Fig 1. 56-year-old white woman with atrophic, porcelain white papules with surrounding rosy erythema and telangiectases of the neck, trunk, and proximal extremities.

mild vacuolar change, dermal edema with mucin, and a sparse perivascular infiltrate (Fig 2, *A* and *B*). Following open discussion in an academic setting, the diagnosis of Degos' disease was proffered. Additional laboratory studies, including anticardiolipin antibody and lupus anticoagulant remained negative.

She was lost to follow-up for 2 years. She reportedly failed thalidomide and suffered a cerebrovascular event at an outside institution while taking this medication. Combination treatment with dipyridamole and aspirin was commenced on next contact.

The patient remained stable without new lesions for 30 months. In July 2002, she suffered a fatal pulmonary embolus.

Case 2

A 40-year-old woman was referred for mildly pruritic papules of the trunk and proximal extremities. The eruption began 18 months earlier on the right thigh. Each lesion proceeded through a proscribed evolution, eventuating as porcelain-white, atrophic scars with a rim of erythema and telangiectases.

The patient remained otherwise healthy. Past medical history was significant for two uncomplicated pregnancies, and a single first-trimester miscarriage. The patient used no medications, vitamins, or supplements.

Biopsy revealed a wedge-shaped area of necrosis in the dermis with abundant mucin deposition (Fig

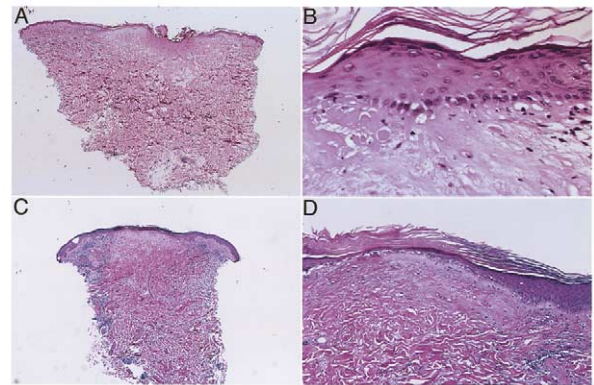


Fig 2. **A,** Case 1. Low-power photomicrograph demonstrates a wedge-shaped infarct in the dermis. Mucin is more apparent with colloidal iron. **B,** Case 1. High-power photomicrograph demonstrates a sparse perivascular lymphocytic infiltrate with mild vacuolar change at the dermoepidermal junction. **C,** Case 2. Low-power photomicrograph demonstrates a wedge-shaped infarct in the dermis. **D,** Case 2. High-power photomicrograph demonstrates a wedge-shaped sparse perivascular lymphocytic infiltrate with mild vacuolar change at the dermoepidermal junction.

2, *C* and *D*). The overlying epidermis was atrophic. Mild dermoepidermal interface change was noted centrally. There was a sparse superficial perivascular infiltrate of lymphocytes. Immunofluorescence studies were unremarkable.

Colonoscopy, esophagogastroduodenoscopy, and ophthalmologic examination were within normal limits. Magnetic resonance imaging (MRI) examination of the head and brain was appropriate for age and health.

ANA was positive at a dilution of 1:320. ENA was negative. IgG antiphospholipid antibodies were present at 39.8 IgG phospholipid level (GFU)/mL. Complete blood cell count (CBC), basic electrolytes, blood urea nitrogen (BUN)/creatinine, liver enzymes, urinalysis, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) were within normal limits.

Treatment was initiated with 325 mg aspirin daily. In 30 months of follow-up, no new lesions have developed and her general health has continued.

Case 3

A 63-year-old woman was referred for multiple slightly pruritic papules of the trunk and proximal extremities. The eruption began 24 months earlier and additional lesions developed in sequential fashion. Each lesion proceeded through a proscribed evolution, to eventuate as porcelain-white, atrophic papules with a rim of rosy erythema.

Table I. Summary of salient features from cases 1-4

Case No.	Age (y)/ Sex	No. of lesions	Distribution	Systemic symptoms	APA status	Other findings of connective tissue disease	Course
1	56/F	Hundreds	Neck, trunk, and proximal extremities	Yes	Neg	ANA negative	CVA; died of PE
2	40/F	Dozens	Predominantly truncal	No	Pos	ANA positive	Relative health
3	63/F	Dozens	Trunk and proximal extremities	No	Neg	ANA positive	Relative health
4	39/F	Dozens	Trunk and proximal extremities	No	Neg	ANA positive; dermatomyositis	DM controlled; relative health

ANA, Antinuclear antibodies; APA, antiphospholipid antibodies; CVA, cerebrovascular accident; DM, dermatomyositis; PE, pulmonary embolus.

The patient remained otherwise healthy. A review of systems was unremarkable. Past medical history was significant for mild hypertension. The patient used no medications, vitamins, or supplements.

Biopsy revealed a wedge-shaped area of necrosis in the dermis with abundant mucin deposition, mild dermoepidermal interface change with occasional necrotic keratinocytes, and a sparse superficial perivascular infiltrate of lymphocytes. The histology was essentially identical to that of Cases 1 and 2.

ANA was positive at a dilution of 1:160. ENA was negative. Antiphospholipid antibodies were not detected. CBC, basic electrolytes, BUN/creatinine, liver enzymes, urinalysis, complement, ESR, and CRP were within normal limits.

Treatment was initiated with aspirin and dipyridamole and she has remained stable through 7 months of follow-up.

Case 4

A 39-year-old woman was referred for small mildly erythematous papules on the proximal upper and lower extremities of four months duration. The patient noted that these papules would appear in crops and heal as small white scars.

Five years earlier, she had developed a photodistributed rash consistent with amyopathic dermatomyositis. She had never demonstrated weakness or objective measures of muscle involvement. Cancer screening had failed to reveal a malignancy. Azathioprine had been used in the past to control her dermatomyositis.

Skin examination revealed Gottron's papules on the knuckles and tendon streaking. Dilated capillary loops were present on the proximal nailfolds. Violaceous macular erythema was present in a shawl distribution. ANA was positive at a 1:320 dilution, muscle enzymes and basic chemistries were normal. Antiphospholipid antibodies were not detected.

A skin biopsy demonstrated incipient focal necrosis, epidermal atrophy, vacuolar interface change,

dermal mucin and a superficial perivascular lymphocytic infiltrate. In some sections, focal thrombosis of blood vessels with smudging of erythrocytes within the lumen was evident.

Daily aspirin was added to her current regimen. With 16 months follow-up, the patient has not noted any new lesions.

A tabular summary comparing all 4 cases is provided (Table I).

DISCUSSION

Degos' disease, also known as malignant atrophic papulosis, is an uncommon condition with reportedly stereotypical skin lesions consisting of largely asymptomatic, porcelain-white, atrophic papules, with surrounding erythema and telangiectases.¹³⁻¹⁵ While the etiology is unknown, evidence suggests a vaso-occlusive process. It has been alternatively regarded as an obliterating arteriolitis, necrotizing vasculitis, endovasculitis with secondary thrombosis, intravascular coagulation disorder, or disorder of fibrinolysis.^{1,2,16-20}

There are no laboratory results pathognomonic of Degos' disease. Diagnosis rests largely on clinical and microscopic findings. Light microscopy classically demonstrates a wedge-shaped zone of necrosis extending from the epidermis to the reticular dermis, mild dermoepidermal interface change, scattered necrotic keratinocytes, dermal edema with copious mucin deposition, sparse perivascular lymphocytic infiltrates, and proliferating endothelial cells with thickened vessel walls and occasional thrombosis. Results of direct immunofluorescence have been inconsistent.^{21,22} Electron microscopy occasionally demonstrates tubuloreticular aggregates within endothelial cells. These inclusions have been postulated to be of viral origin or, alternatively, equated to those seen occasionally in lupus erythematosus.^{3,23}

Lesions follow a proscribed evolutionary sequence, which must be considered during interpretation of clinical and histological data. It is interesting to note that at some point in their course, each

patient had a biopsy which demonstrated a perivascular inflammatory infiltrate, copious dermal interstitial mucin, and focal vacuolar alteration of basal keratinocytes; features which are shared by lupus erythematosus, dermatomyositis, and Degos' disease.

Speculation that lupus and antiphospholipid antibodies may be involved in the pathogenesis, as recently suggested by Ball and Ackerman et al,²⁴ is appealing, particularly when one considers that ANA and antiphospholipid antibody testing has been widely available only since the mid-1960s and mid-1980s, respectively. Early cases of Degos' disease may simply represent poorly characterized connective tissue disease, particularly that of lupus erythematosus. Nevertheless, Assier et al²⁵ reported the absence of antiphospholipid antibodies in a study of 15 patients with Degos' disease, indicating that further study is necessary. In the cases outlined herein, ANA positivity and antiphospholipid antibodies represent clear points of differentiation despite strong similarity in clinical and histological findings.

Since the mid-1980s there have been reports of cutaneously-limited variants of Degos' disease.^{3,4} Such cases have often demonstrated a strong hereditary component.^{5,6} Investigators have estimated that approximately 4-15% of patients with lesions consistent with Degos' disease enjoy continued relative health.^{3,4,21,26} While it is impossible to predict with certainty which patients will progress to fulminate disease, evidence suggests a lack of visceral involvement two years after diagnosis portends a better prognosis.^{15,27}

These reports, in aggregate, stand in contrast to the classic description of malignant atrophic papulosis, further confounding a rare and poorly understood disease process. Lupus erythematosus is a disease process known to have great variance in presentation and extent of involvement. Perhaps, Degos' disease is best thought of along these same lines, or perhaps, even within them.

Furthermore, it is interesting that the patient detailed in Case 1 suffered a cerebrovascular event while on thalidomide therapy. Thrombotic events have been described in patients with lupus erythematosus while on thalidomide. Those who manifest this side effect appear to have underlying risk for thrombosis such as a lupus anticoagulant or antiphospholipid antibody.^{28,29,30} Risk of thrombosis such as is seen in classic malignant atrophic papulosis should be a contraindication to thalidomide therapy as well.

Treatment of Degos' disease has varied widely depending on the suspected etiology. Anticoagulation with heparin has been utilized in the acutely

ill.³¹ Other anticoagulation strategies with coumadin have been unsuccessful.³² Fibrinolytics such as phenformin and ethylestrenol have yielded mixed results.^{33,34} Other largely unsuccessful therapies have included sulphonamides, streptomycin, tetracycline, penicillin, corticosteroids, arsenic, chloroquine, azathioprine, methotrexate, low molecular weight dextran, and phenylbutazone.^{14,34} A substantial number of cases have responded well to aspirin and dipyridamole.^{3,26,35,36}

CONCLUSION

In summary, we propose that Degos' disease is, perhaps, not a distinct clinical entity, but rather that it represents a common clinical and histological endpoint to vascular insult. Considerable blurring and incomplete characterization of the original defining cases of malignant atrophic papulosis exist. It is likely that many historical cases were associated with antiphospholipid antibody and/or lupus erythematosus; however, confirmatory testing was not then available. We assert that several different disease processes may converge to produce what were formerly considered nearly pathognomonic clinical and histological findings.

Accordingly, the clinical and histological findings of Degos' disease might better be described as a reaction pattern, and when present, investigation into associated or mimicking conditions should be commenced, including studies for lupus erythematosus, dermatomyositis, and antiphospholipid syndromes, to name a few.

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