

Lesions Resembling Malignant Atrophic Papulosis in a Patient With Progressive Systemic Sclerosis

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Malignant atrophic papulosis (MAP), or Degos syndrome, is a rare disorder of unknown etiology. It is characterized by a deep subcutaneous vasculopathy resulting in atrophic, porcelain-white papules. We report the case of a 42-year-old woman with a history of progressive systemic sclerosis who presented with painful subcutaneous nodules on her abdomen along with chronic atrophic papules on her upper and lower limbs. Biopsy results of both types of lesions revealed vascular thrombi without surrounding inflammation. We briefly review the literature on MAP and its association with various connective tissue diseases. To our knowledge, there have been no previous reports of a patient with the clinical and histologic presentations described here. Although the histologic appearance of the subcutaneous nodules was very similar to that of the atrophic papules, the clinical characteristics of the 2 types of lesions were strikingly different. It is fair to theorize that Degos lesions do not start as atrophic porcelain-white papules but rather evolve from a primary lesion. We hypothesize that these lesions start as painful red nodules and may represent part of the disease spectrum in the evolution of MAP.

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Malignant atrophic papulosis (MAP), or Degos syndrome, is characterized as a vasculopathy of unknown etiology. Described by Degos and colleagues¹ in 1942, the disease presents as multiple porcelain-white erosions. Associated symptoms often include abdominal pain, gastrointestinal

bleeding, and neurologic deficits. The prognosis is usually poor. Histologic characteristics include a vasculopathy below the necrobiotic zone with endothelial swelling, proliferation, and thrombosis. To our knowledge, only a few cases of MAP associated with connective tissue disease have been reported: 4 cases with systemic lupus erythematosus, 1 with dermatomyositis, and 1 with progressive systemic sclerosis.²⁻⁵ We present the case report of a woman with progressive systemic sclerosis and MAP-like lesions.

Case Report

Round erosions with dry central crusts developed on a 42-year-old woman with a long history of progressive systemic sclerosis, significant pulmonary hypertension, and right heart failure. Although the lesions were scattered on all limbs, the most prominent lesions extended from the right labium majus down the anterior aspects of both limbs. Associated symptoms included mild pruritus.

One month after the appearance of these lesions, painful subcutaneous nodules developed on the patient's abdomen in a background of mild diffuse erythema. The nodules were exquisitely tender on palpation. Abdominal pain was confined to the area of the cutaneous lesions. The patient denied any fever, chills, diarrhea, nausea, or vomiting. In addition to progressive systemic sclerosis, the patient's medical history included iron deficiency anemia, restless legs syndrome, gastroesophageal reflux disease, and depression. Her medications included trestatinil (UT-15, an experimental prostaglandin used to treat her pulmonary hypertension), levothyroxine, lansoprazole, sertraline, furosemide, spironolactone, and hydromorphone hydrochloride. There were no known drug allergies.

Significant findings from the physical examination included a mask with multiple matted telangiectasias and cyanosis. The phalanges were firm and sclerotic with marked cyanosis. On the lower

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abdomen, there was a dull red erythema with multiple exquisitely tender nodules measuring approximately 10×10 mm. Multiple scattered round erosions about 5 mm in diameter with dry central crusts were noted on the right labium majus, upper arm, and anterior aspect of the lower limbs (Figure 1). These lesions were not painful on palpation. No neurologic abnormalities were elicited on examination.

The patient was admitted to the hospital with a possible diagnosis of cellulitis or panniculitis and started on treatment with imipenem. Results of a computed tomography scan did not reveal any evidence of necrotizing fasciitis. Abnormal laboratory values included an α_1 -antitrypsin level of 416 mg/dL and aldolase level of 8.7 U/L. Results of serum protein electrophoresis showed an albumin level of only 2.9 g/dL and an elevated α_1 -globulin level of 0.54 g/dL. Results of a cryoglobulin assay were normal.

Punch biopsies of the lower limb lesions and abdominal nodules were performed. Fat necrosis with a predominant histiocytic inflammation surrounding adipocytes was seen in both tissue samples. Also noted on the lower limb sample was a wedge-shaped, full-thickness, epidermal ulceration with mild to moderate neutrophilic inflammatory diapedesis consistent with the clinical findings of erosive lesions with dry crusts. In addition, the histologic findings included vascular thrombi without surrounding inflammation, as is seen in MAP. There was no evidence of panniculitis or cellulitis. Because the same histopathologic process was documented in strikingly disparate clinical presentations, biopsies were repeated. An incisional biopsy of the abdominal nodules and a punch biopsy of lesional and perilesional areas of the lower limb also provided evidence of a vasculopathic process with thrombi and deep dermal hemorrhage in the adipose tissue (Figures 2–4).

The histologic findings supported a diagnosis of scleroderma-associated vasculopathy, and antibiotic treatment was discontinued. A review of the literature suggested that antiplatelet therapy might provide some therapeutic benefit.^{6,7} However, because treprostinil is a potent platelet antagonist, no new treatment was prescribed. Following a pain management consultation, the patient was discharged. Her abdominal and lower extremity lesions have not improved.

Comment

We report the development of a vasculopathy, which was histologically similar to MAP, that developed in a woman with classic progressive systemic



Figure 1. Necrotic atrophic papule on the lower limb of a 42-year-old woman.

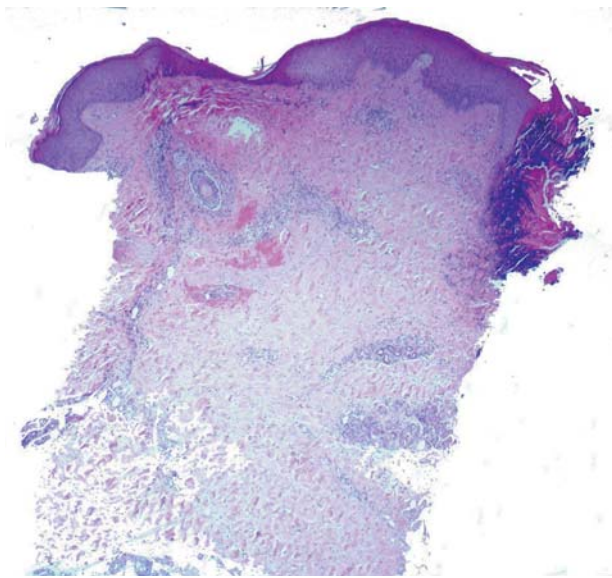


Figure 2. Crusted necrotic papule with wedge-shaped architecture on the proximal thigh. Full-thickness epidermal ulceration, mild neutrophilic inflammatory diapedesis, and deep dermal hemorrhage (H&E, original magnification ×20).

sclerosis. In addition to the atrophic papules characteristic of MAP, the patient also presented with tender subcutaneous nodules with histologic features identical to those of MAP lesions. The pathogenesis of MAP is unknown. In addition to the cutaneous manifestations, abnormalities in the gastrointestinal, neurologic, cardiac, and urinary systems have been reported.⁸ The poor prognosis is often a result

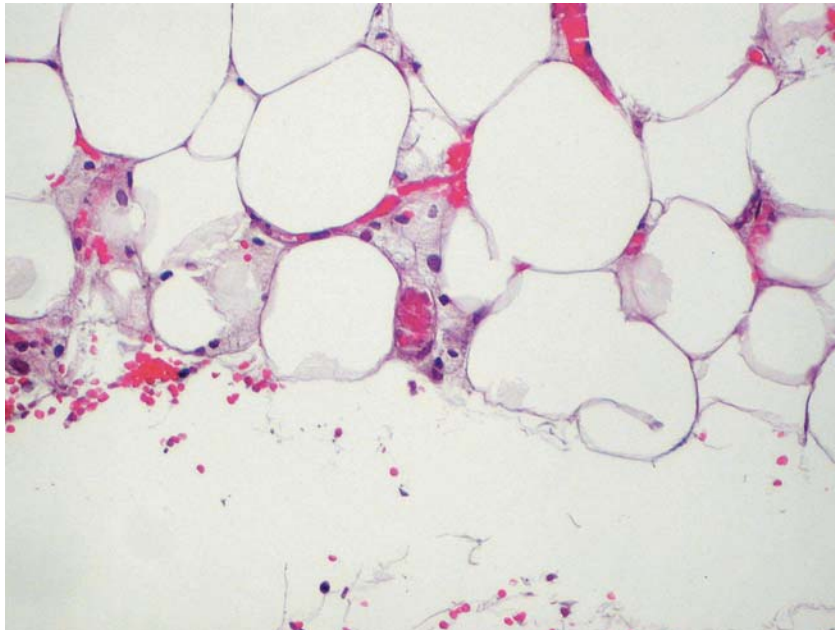


Figure 3. Early fat necrosis and numerous small vessels occluded by hyaline thrombi at the dermal-subcutaneous interface of a proximal thigh lesion, consistent with vasculopathy (H&E, original magnification $\times 100$).

of gastrointestinal bleeding or intestinal perforation. However, disease that is limited to the skin may have a more benign course.⁹

The literature on the association between connective tissue disease and MAP is limited; to our knowledge, there are only 4 cases associated with systemic lupus erythematosus and 1 case each with dermatomyositis and progressive systemic sclerosis.²⁻⁵ Of the 6 reported cases, 5 occurred in women. The exception was a case of MAP in an African American man with progressive systemic sclerosis that was reported by Durie and colleagues.⁵ In this case, the lesions originated on the face, then progressed to involve the arms, chest, shoulders, and abdomen. The lesions were neither painful nor pruritic. No subcutaneous lesions were found. The patient died of fulminant progressive systemic sclerosis, and his death was not attributed to MAP.⁵

Durie and colleagues⁵ questioned whether the association between MAP and progressive systemic sclerosis was a coincidence or whether it represented an underlying pathologic process common to both disorders. Owing to our limited understanding of both disorders, we can only look to past histopathologic studies to guide us. MAP is characterized by vascular damage predominantly to the arterioles but including some deep venules.⁸ The histopathologic features include vasculopathy below the necrobiotic zone and endothelial swelling, proliferation, and thrombosis. There is often an absence of inflammation in the adnexa and superficial vasculature, especially in early lesions. The vessel lumen is narrowed by endothelial proliferation and obstructed by a thrombus. The media and adventitia are not

affected but may be edematous. The area around the vessels is usually paucicellular. In later stages, as dermal ischemia ensues, a mild to moderate inflammatory diapedesis of lymphocytes may develop, rimming the periphery of ischemic tissue. Other than fat necrosis in the abdominal lesion, no other significant inflammatory insult was documented in our patient; this finding suggests that the presentation in this patient represented an early stage of a vasculopathic process common to MAP.^{8,10}

The histologic features of vasculopathies in scleroderma, especially in the setting of Raynaud syndrome, have been well-described.¹¹⁻¹³ Vessels of all sizes can be affected. In addition, serum levels of factor VIIIIR (von Willebrand factor) and endothelin 1 are significantly elevated in some patients; these elevations lead to endothelial cell damage and intimal proliferation. Plasminogen activator release is also diminished, resulting in a prothrombotic state that exacerbates the pathologic process initiated by luminal narrowing. The source of this abnormal endothelial response is often Raynaud phenomenon, in which a vasculopathy leads to ischemic and reperfusion injury to the skin.¹³ The porcelain-white cutaneous infarcts of MAP most likely represent the extreme spectrum of these vasculopathic changes.

Given the similar histologic presentations of various vasculopathic lesions, Durie and colleagues⁵ concluded that MAP is a diagnosis of exclusion. The cutaneous vasculopathies represent a common end point of multiple pathologic processes. Cutaneous infarcts in collagen vascular diseases such as systemic lupus erythematosus and

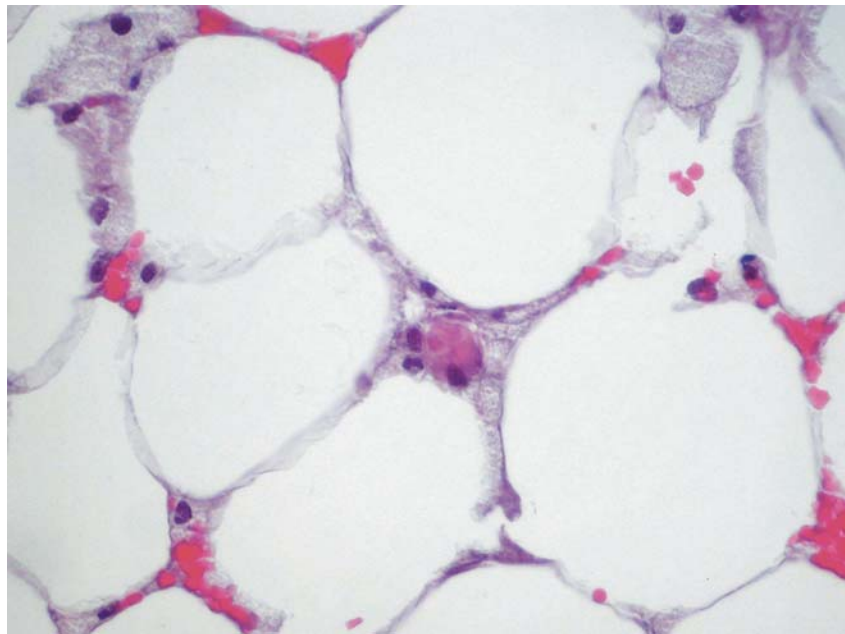


Figure 4. Similar hyaline thrombi and subtle alteration of adipocyte architecture within the subcutaneous fat seen in a tissue sample of an abdominal lesion (H&E, original magnification $\times 400$).

scleroderma are probably a sequelae of their respective autoimmune disorders; they are not MAP as described by Degos. We agree with the conclusion of Dubin and Stawisk² that a diagnosis of MAP and its associated gastrointestinal complications or morbidity cannot be made if an underlying autoimmune process has not been ruled out. Moreover, we suggest that, given the similar underlying vasculopathic processes in autoimmune disorders and MAP, there is a continuum of histologic and clinical changes, with lesions resembling MAP representing the most serious sequelae of the dermal vasculopathy.

A fascinating aspect of this case was the strikingly different clinical presentations of the leg and abdominal lesions. None of the previous case reports included tender subcutaneous nodules. These lesions may represent the initial manifestations of MAP, which later progress into necrotic erosions. Another possibility is that the subcutaneous lesions may signify a more restricted vasculopathic process. The antiplatelet therapy in our patient may have limited the ischemic injury to overlying skin. Necrosis occurs only when a significant number of blood vessels have been compromised. Because anticoagulation/antiplatelet therapy is used in certain connective tissue diseases, tender subcutaneous nodules should be considered part of the disease spectrum in MAP.

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