A Huge Pyoderma Gangrenosum-like Lesion as a Presenting Sign of Antiphospholipid Antibody Syndrome

To the Editor:

The antiphospholipid antibody syndrome (APS) is associated with various cutaneous manifestations¹ and leg ulceration is one of the most common. Cutaneous ulcers presenting as pyoderma gangrenosum (PG) have rarely been reported in this setting. Schmid, *et al*² described a 64-year-old woman with systemic lupus erythematosus who presented with 2 large nonhealing ulcers on her right shank. PG associated with secondary APS was diagnosed². Chacek, *et al*³ reported a 28-year-old man with PG and inferior vein syndrome due to thrombosis. A prolonged partial thromboplastin time and a positive test for circulating anticardiolipin antibodies led to the diagnosis of APS³. Schlesinger, *et al* reported 2 cases with an association between primary APS and PG-like skin lesions⁴.

We describe a young man with a PG-like skin lesion. After evaluation to rule out PG-associated disorders, he was diagnosed with primary APS based on increased antibodies to cardiolipin and biopsy results. The ulcer healed completely.

A 48-year-old Caucasian man presented with a necrotic ulcer in his right shank that had appeared a week before admission. He reported a recent minor trauma to this leg. He also mentioned skin ulcers in his right elbow and left leg 30 years earlier that were treated with antibiotics and skin transplantation. He was transferred to our department from orthopedics after the lesion worsened under parenteral antibiotic therapy.

Examination revealed good general condition, no signs of sepsis, no systemic fever, vitiligo on the chest, and old scars from skin transplants. An 8×11 cm ulcer with a bleeding base and necrotic borders was observed on the right shank (Figure 1). Peripheral pulses were normal. The presumed clinical diagnosis was PG.

White blood cell count was 21.41×10^9 /l, hemoglobin 14.3 g/dl,



Figure 1. PG-like skin lesion prior to therapy.

platelets $286 \times 10^9/l$, albumin 3 g/dl, and globulins 2.6 g/dl. Renal and liver function tests were normal. Coagulation assays including prothrombin time and partial thromboplastin time were normal, as was protein serum electrophoresis. Blood cultures and cultures taken from the ulcer edge were all negative. A colonoscopy was performed to rule out inflammatory bowel disease (IBD) and no evidence of colitis was found. Five benign polyps were resected from the rectum and sigmoid colon.

Anticardiolipin antibodies required to rule out a PG-like lesion were positive, with IgG 96.7 U/ml. IgM and lupus anticoagulant antibodies were negative. Six weeks later, the IgG titer was still positive (21.8 U/ml). Screening for antinuclear antibodies, rheumatoid factor, cryoglobulins, antineutrophil cytoplasmic antibodies, C3, and C4 were all negative and the condition was classified as a primary APS. A biopsy revealed a thrombus occluding the vascular lumen (Figure 2). Our clinical diagnosis was a skin ulcer presenting as PG, secondary to primary APS. The patient was given low molecular weight heparin (LMWH) injections (enoxaparin 80 mg twice a day for 30 days, which was reduced to 80 mg once a day), with dramatic clinical improvement. He was also treated with steroids (prednisone 60 mg with gradual tapering for 6 weeks). The ulcer healed completely within 2 months and the leg remained healthy a year later (Figure 3). Anticardiolipin antibodies remained elevated above 120 U/ml.

Pyoderma gangrenosum is an ulcerative disease of the skin of unknown origin. Roughly half the cases are associated with an underlying systemic disease, most commonly IBD, arthritis, or a lymphoproliferative disorder^{5,6}. There are no pathologic or laboratory findings that are pathognomonic for PG.

In patients initially diagnosed with PG, a misdiagnosis rate of up to 10% has been reported⁷. The investigators also revealed that APS associated with PG may be difficult to diagnose because of the low specificity of histologic findings and its frequent response to systemic corticosteroids⁷. Less than one-third of cases showed histologic evidence of a coagulopathy, while about 60% of patients improved with systemic corticosteroids, which accounted for the greater delay before a final diagnosis of APS, compared to other causes of ulceration⁷.

In our patient, a thorough examination (including biopsy) was performed to rule out diagnoses mimicking PG. Primary APS was confirmed by positive serology in combination with suggestive histopathological features.

APS is a systemic autoimmune disorder characterized by arterial and/or venous thrombosis, recurrent fetal loss, thrombocytopenia, and the presence of antiphospholipid antibodies. Standard therapy for thrombosis in patients with APS commonly consists of heparin, followed by warfarin⁸.

We treated the patient with LMWH because of its antiinflammatory effects. LMWH preferentially inhibits tumor necrosis factor- α and interleukin 4 (IL-4) production. *In vivo*, subcutaneous injections of LMWH inhibit leukocyte infiltration associated with a late cutaneous response⁹. Use of LMWH, but not unfractionated heparin, leads to a dose-dependent increase in IL-6 from nonstimulated peripheral blood mononuclear cells isolated from healthy donors¹⁰.

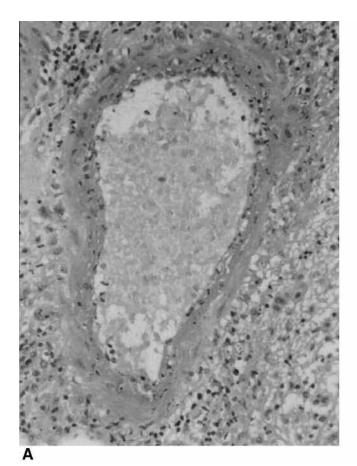
We recommend investigation for APS in all patients presenting with PG-like skin lesions, and also consideration of longterm LMWH therapy when the diagnosis is established.

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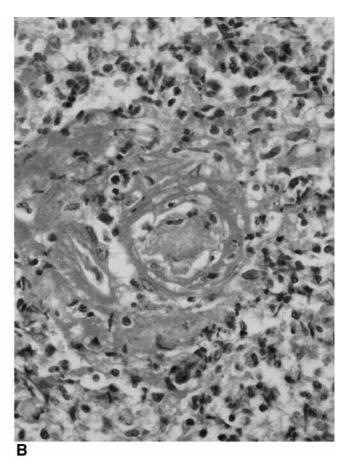


Figure 2. A. The skin lesion biopsy reveals fibrin. B. Thrombus-containing fragmented blood cells occlude the vascular lumen.



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Figure 3. The cured ulcer a few weeks after LMWH therapy was ended.

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