SKIN

BRIEF ARTICLE

Necrotic Leg Nodules as the Initial Cutaneous Manifestation of Multi-System Granulomatosis with Polyangiitis

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ABSTRACT

Granulomatosis with polyangiitis (GPA) is an autoimmune vasculitis typically affecting small to medium-sized vessels. Cutaneous findings are varied but classically include those such as palpable purpura and mucocutaneous ulcers. Initial presentation with skin manifestations is associated with worse systemic disease. Here, we describe the challenging diagnosis of a patient with GPA who presented with necrotic leg nodules as the initial clinical cutaneous sign prior to the onset of systemic symptoms. This rare presentation underscores the critical need for dermatologists to consider vasculitic processes when presented with tender leg nodules. We highlight the nuance and important role of dermatological assessments such as biopsies to capture evidence of vasculitis in this context and encourage laboratory testing for vasculitis-associated antibodies, particularly in patients with other vasculitis-associated symptoms.

INTRODUCTION

Granulomatosis with polyangiitis (GPA) is an autoimmune vasculitis characterized by granulomatous inflammation and necrotizing vasculitis affecting small to medium-sized vessels. Patients with GPA may present with nonspecific symptoms, respiratory involvement, and/or rapidly progressing glomerulonephritis, but varied cutaneous manifestations occur in over 50% of patients.[1] Skin lesions infrequently precede the onset of systemic disease.[2] Cutaneous findings typically include palpable purpura and mucocutaneous ulcers; histopathology frequently demonstrates leukocytoclastic vasculitis and necrotizing granulomatous inflammation.[1,3] We report the case of a patient with GPA who presented with necrotic leg nodules as the initial clinical cutaneous sign prior to the onset of her systemic symptoms.

CASE REPORT

A 68-year-old female presented to primary care with bilateral leg nodules and was treated with a 10-day course of doxycycline for presumed cellulitis. She re-presented to the emergency department twice due to lack of improvement, additional right lower extremity nodules, swelling, and redness.

Doppler ultrasound was negative for deep vein thrombosis and labs were within normal limits; CT showed subcutaneous edema and soft tissue stranding concerning for cellulitis, so she was discharged with a 10-day course of trimethoprim-sulfamethoxazole and clindamycin. She again presented a few weeks later reporting new subjective fevers, malaise, weight loss, and abdominal discomfort. Upon dermatology consultation, physical exam was notable for tender erythematous to violaceous indurated nodules with central areas of necrosis and ulceration (**Figure 1**).

Testing was notable for large blood on urinalysis and elevated ESR (66) and CRP (178). Creatinine rose from baseline of 0.6 to peak of 3.3 during inpatient stay. PR3-ANCA was positive (>200) with positive c-ANCA, negative p-ANCA, and negative anti-GBM. Two punch biopsies were performed. Tissue culture, acid fast bacteria, and fungal culture were negative. Histopathology noted septal panniculitis with fibrosis and granulomatous inflammation in both legs and was initially read as erythema nodosum. Renal biopsy showed pauci-immune focal necrotizing and crescentic glomerulonephritis with PR3+ immunofluorescence. Both skin biopsies were then entirely step-sectioned, demonstrating septal panniculitis and granulomatous vasculitis, interpreted as manifestations of GPA (**Figures 2A, B**).

Seven days of cephalexin and doxycycline were initiated to treat inflammation and concern for secondary infection. 3 days of IV methylprednisolone followed by prednisone taper were given due to concern for ANCA-associated vasculitis. Following kidney biopsy, the patient received rituximab and was discharged with Cr down trending to 1.6 and outpatient follow-up. 4 days later, the patient endorsed continued calf pain with redness and subjective improvement in fatigue and malaise. Clobetasol and mupirocin ointments were added to the regimen.

DISCUSSION

Diagnosis of GPA is challenging, and evaluation of cutaneous findings at the time of presentation is complicated by the wide variety of manifestations associated with ANCA-associated vasculitides. However, early recognition is important given that patients with GPA presenting with cutaneous manifestations are more likely to have pulmonary, renal, neurologic, musculoskeletal, and gastrointestinal complications.[4] A large cross-sectional study found that 2.9% of patients with GPA eventually had nonspecific tender skin nodules mimicking panniculitis.[4] Biopsy-proven septal panniculitis has been described in two cases as a potential long-term complication of GPA.[2,5] In contrast, our patient first endorsed leg pain in the setting of evolving, necrotic tender nodules showing septal panniculitis with granulomatous vasculitis on biopsy prior to the onset of subjective systemic symptoms or the discovery of hematuria on urinalysis. Thus, it is important to highlight that tender nodules can rarely present as the initial manifestations of GPA, and skin biopsy can be instrumental in establishing the diagnosis in such cases. Particularly in patients with other vasculitis-associated symptoms, clinicians should consider laboratory testing for vasculitis-associated autoantibodies, re-sectioning existing biopsies, and/or additional biopsies to capture evidence of vasculitis.

Conflict of Interest Disclosures: None

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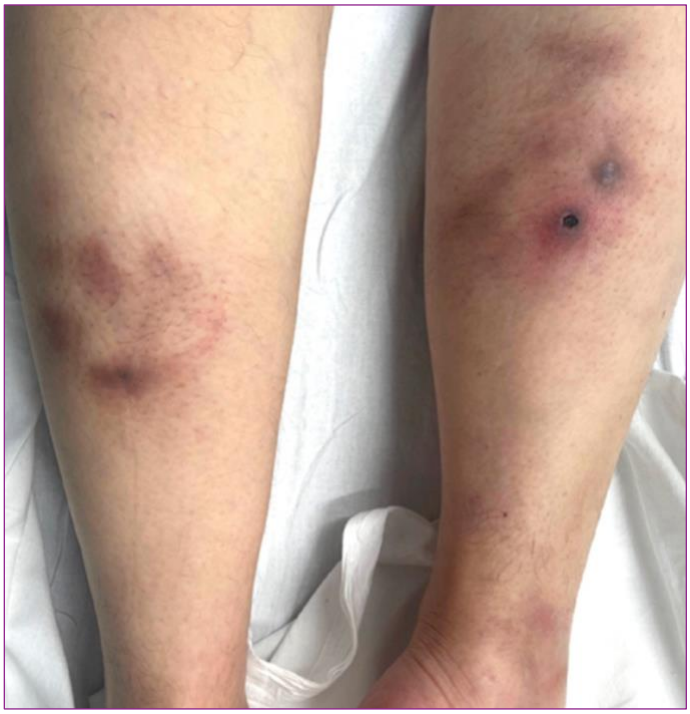

Figure 1. Photographic documentation of the leg nodules with necrotic eschar.

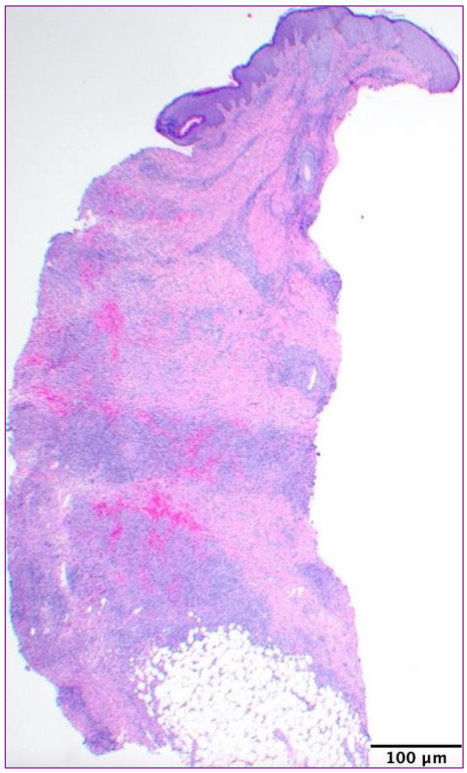

Figure 2A. Histopathology of leg nodules. Scanning magnification of this punch biopsy demonstrates nodular inflammation extending from the superficial dermis to the subcutis, with zones of interspersed hemorrhage. The fibrous septae of the subcutis are expanded, while the fat lobules are generally spared (Hematoxylin and eosin, 20x). Higher power magnification of the deep reticular dermis highlights a dense mixed inflammatory infiltrate with multinucleate giant cells and loose granuloma formation (yellow arrow).

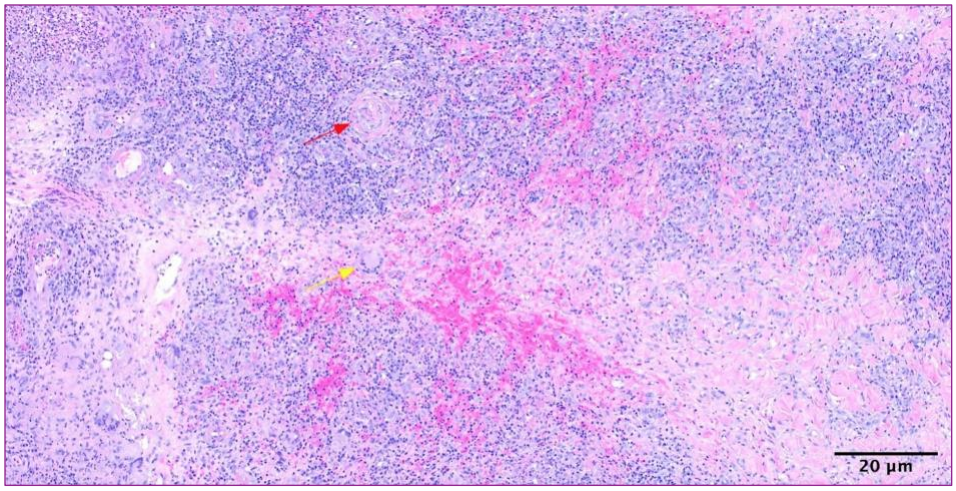

Figure 2B. Several vessels demonstrate prominent perivascular fibrin deposition with neutrophilic infiltrates in vessel walls (red arrow), surrounding hemorrhage, and leukocytoclasis (Hematoxylin and eosin, 100X).

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