

Antineutrophil cytoplasmic antibody positivity and cutaneous IgA vasculitis in a patient with antisynthetase syndrome



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Key words: antineutrophil cytoplasmic antibodies (ANCA)-associated vasculitis (AAV); antisynthetase syndrome; cutaneous vasculitis; leukocytoclastic vasculitis.

INTRODUCTION

Vasculitis is a disease process that results from inflammation of blood vessel walls. The clinical presentation is variable and dependent upon the size and location of the vessels involved.¹ Cutaneous vasculitis refers to a vasculitis that results in skin manifestations, often due to involvement of small- and medium-sized vessels. The incidence of cutaneous vasculitis ranges from 15.4 to 29.7 cases per 1 million people every year.² Clinical presentations vary and can include petechiae, purpura, purpuric papules, hemorrhagic vesicles, and bullae.¹ Biopsy is the gold standard for making a diagnosis of cutaneous vasculitis.² The collection of histopathologic findings in cutaneous small-vessel vasculitis are referred to as leukocytoclastic vasculitis (LCV) and include a polymorphonuclear neutrophilic infiltrate, primarily in postcapillary venules, with fibrinoid deposits in and around the vessel wall and extravasation of red blood cells.³ Although LCV is often idiopathic, it may occur secondary to infection, drugs, malignancy, or autoimmune processes, such as antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV).⁴ The following case report describes a patient with a history of antisynthetase syndrome (ASS) who subsequently developed IgA vasculitis with copositive ANCA.

CASE REPORT

A 34-year-old Hispanic woman with ASS presented to the dermatology clinic with a 1-month history of painless, nonpruritic purpuric macules and

Abbreviations used:

AAV:	ANCA-associated vasculitis
ANCA:	antineutrophil cytoplasmic antibodies
ASS:	antisynthetase syndrome
LCV:	leukocytoclastic vasculitis

scattered purpuric papules that started on the bilateral shins and progressively extended to involve the abdomen, buttocks, and bilateral lower extremities. She had been diagnosed with ASS 2 years prior to presentation; findings at that time included intermittent and worsening joint pains with negative ANCA, interstitial lung disease, mild mechanic's hand changes to her right second finger, elevated erythrocyte sedimentation rate, creatinine kinase, and positive anti-PL-7 antisynthetase antibody.

Skin examination revealed purpuric macules and scattered purpuric papules (Fig 1). Urinalysis revealed proteinuria and hematuria. Skin biopsy demonstrated superficial perivascular and interstitial mixed inflammatory infiltrate comprised of neutrophils, eosinophils, and lymphocytes in the dermis, extensive leukocytoclasia, and prominent hemorrhage (Fig 2). Superficial hyaline thrombi and focal fibrinoid necrosis of the small vessel walls were also scattered throughout. Direct immunofluorescence showed fibrin, C3, and IgA deposits in the superficial vessels. Laboratory testing was positive for perinuclear ANCA (1:320) and antimyeloperoxidase antibodies (2.7 AI).

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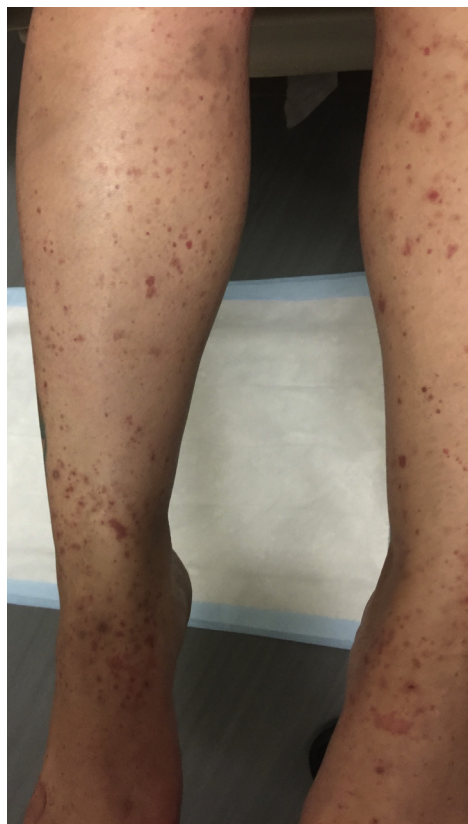


Fig 1. Purpuric macules and papules overlying the lower extremities bilaterally.

A few weeks after presentation, the patient developed dyspnea, chest tightness, and hemoptysis, requiring hospitalization. A basic metabolic panel revealed an elevated serum creatinine concentration of 1.39 mg/dL (baseline 0.9 mg/dL). Bronchoscopy with bronchoalveolar lavage revealed diffuse alveolar hemorrhage localized to the left upper lobe. During hospitalization, the patient received 3 doses of intravenous methylprednisolone and 1 dose of rituximab. After 3 days of hospitalization, she was discharged on a short tapered course of oral methylprednisolone and prophylactic trimethoprim/sulfamethoxazole. The following month, repeat ANCA and antimyeloperoxidase titers remained elevated, at 1:160 and 1.0, respectively.

DISCUSSION

The patient's cutaneous presentation along with the histopathologic findings of LCV are consistent with the diagnosis of cutaneous vasculitis. This patient's presentation of cutaneous vasculitis associated with diffuse alveolar hemorrhage and hematuria is consistent with systemic vasculitis.

AAV refers to a group of vasculitides associated with ANCA that trigger inflammation of small- and

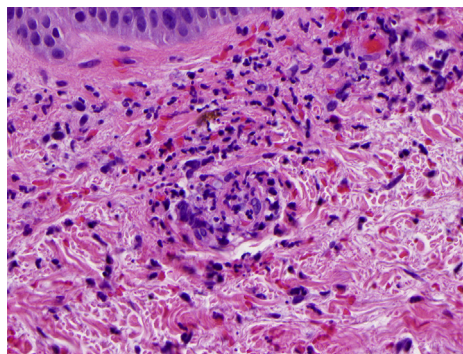


Fig 2. Skin biopsy demonstrating superficial perivascular and interstitial mixed inflammatory infiltrate comprising neutrophils, eosinophils, and lymphocytes in the dermis. (Hematoxylin-eosin stain; original magnification: $\times 400$.)

medium-sized vessels. Common organs affected by AAV include the skin, kidneys, and lungs, presenting as palpable purpura, glomerulonephritis, and pulmonary hemorrhage, respectively; these were seen in this patient's presentation.⁵ LCV can accompany systemic AAV; a study by Aurora et al³ analyzed 84 patients with cutaneous LCV proven by biopsies and found that 8 (10%) of them had AAV. Of note, this patient had a negative test for ANCA antibodies 2 years prior.

Interestingly, direct immunofluorescence also showed IgA deposition in the superficial vessels. Typically, AAV is pauci-immune on direct immunofluorescence, with IgA depositions being more suggestive of IgA vasculitis. Both AAV and IgA vasculitis can present similarly in the skin, as both can affect the superficial vasculature. AAV is more known to affect cutaneous medium-sized vessels, leading to systemic vasculitis. Overlap syndromes have been described in patients with features of both conditions.⁶

A study by Kim et al⁷ demonstrated that patients with IgA vasculitis and copositive ANCA exhibited higher rates of pulmonary and nervous involvement than those with IgA vasculitis and negative ANCA. This case reinforces that patients with IgA vasculitis with positive ANCA are at higher risk of lung involvement, as this patient developed pulmonary hemorrhage in the setting of chronic immunosuppression for ASS.

ASS is an autoimmune disorder that presents clinically with myopathy, inflammatory arthritis, fever, Raynaud disease, and interstitial lung disease. Lab findings include positive titers for antibodies directed against an aminoacyl transfer RNA synthetase.⁸ In the literature, there is only 1 case of a patient who developed an apparent idiopathic cutaneous vasculitis but was found to have positive

antiglycyl tRNA synthetase antibodies in the serum, despite any previous signs, symptoms, or diagnosis of ASS. In our case, at the time of presentation, the patient had been on chronic immunosuppression (methylprednisone 4 mg daily and mycophenolate mofetil 2 g daily) for over a year; this regimen kept her symptoms of ASS under good control for several months. Our literature review revealed no reported cases documenting patients on chronic immunosuppression for ASS in whom vasculitis subsequently developed. Immunosuppressive medications including systemic steroids are used to treat cutaneous and systemic vasculitis.

While the etiology of vasculitis is often idiopathic and challenging to identify, it is of vital importance. Workup of these patients should be directed to identifying causal agents and evaluating organ systems to assess the extent of involvement and prevent development of severe complications.

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Conflict of interest

None disclosed.

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