

Paraneoplastic microscopic polyangiitis presenting after thymectomy



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INTRODUCTION

Thymoma is the most common neoplasm of the thymus, and early-stage tumors carry an excellent prognosis with 5-year survival rates over 85% with primarily surgical management.¹ However, thymoma has a strong association with paraneoplastic syndromes, which do not have the same favorable response to surgery. Paraneoplastic syndromes are found to persist, worsen, or even present in the post-thymectomy setting. We report a case of likely paraneoplastic vasculitis in the setting of thymoma that presented after thymectomy.

CASE

A previously healthy 60-year-old man presented to an outside hospital with recurrent pruritic eruptions in the setting of unintentional weight loss, diffuse arthralgias, and myalgia. The eruptions were characterized by pink papules on his trunk and proximal thighs that resolved within 24 hours with no hyperpigmentation, clinically consistent with urticaria. He was treated with prednisone, up to 40 mg daily, and his rash flared when the dose was tapered. Chest radiograph showed a large mediastinal mass found to be a stage IIb thymoma. The mass was excised, and he underwent postoperative radiation therapy. The patient's urticaria improved postoperatively, but he required prednisone, 10 mg daily, to maintain disease control. Biopsy results of the transient urticarial rash were consistent with urticaria with no signs of vasculitis.

Three months postoperatively, the patient noted worsening of his rash and persistence of lesions beyond 24 hours. He presented to our department

Abbreviations used:

MPA:	microscopic polyangiitis
pANCA:	perinuclear antineutrophil cytoplasmic antibody
UV:	urticarial vasculitis

with blanchable, edematous, erythematous papules admixed with hyperpigmented ecchymotic patches (Fig 1). Punch biopsies were performed, and the patient was started on cetirizine and ranitidine and maintained on prednisone. Histology found a predominantly neutrophilic infiltrate, leukocytoclasia, and occasional eosinophils. Dermal hemorrhage was present as was focal vessel wall damage. The histologic features were consistent with an early lesion of urticarial vasculitis (Fig 2).

Laboratory results found a modest elevation in creatinine to 1.1 mg/dL from a baseline of 0.8 (to convert to micromoles per liter, multiply by 88.4), an erythrocyte sedimentation rate of 30 mm/h, C-reactive protein level of 3.3 mg/dL (to convert to nanomoles per liter, multiply by 9.524), and low C3 and C4 levels of 82 mg/dL and 14 mg/dL, respectively (to convert to grams per liter, multiply by 0.01). Thyroid-stimulating hormone and free thyroxine levels were within normal limits. Serologic testing results were positive for perinuclear antineutrophil cytoplasmic antibody (pANCA) with antimyeloperoxidase specificity and negative for rheumatoid factor, anti-Ro, anti-La, and hepatitis B and C. Microscopic hematuria prompted a retroperitoneal ultrasound scan, which found no hydronephrosis or calculi, and renal biopsy was deferred because of lack of proteinuria, dysmorphic red blood cells, and

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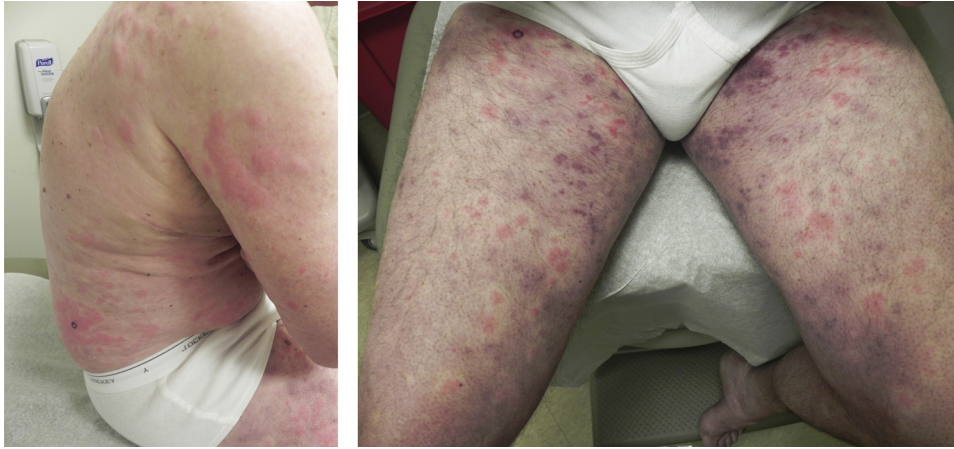


Fig 1. MPA clinical photographs. Blanchable, edematous, erythematous papules admixed with hyperpigmented ecchymotic patches.

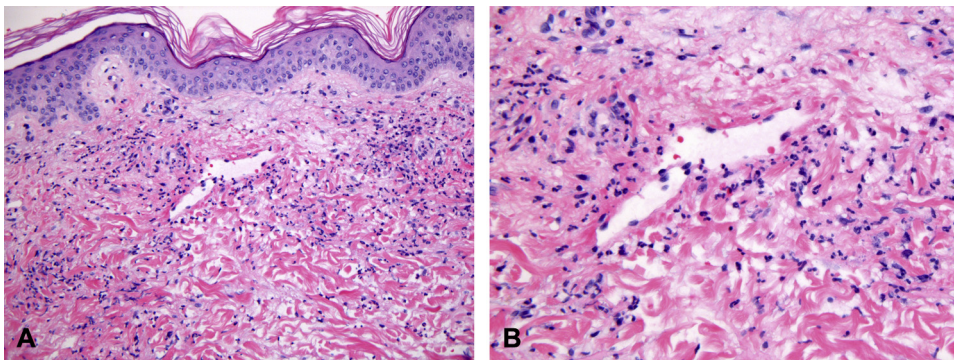


Fig 2. MPA histologic findings. **A**, Low-power view shows focal dermal hemorrhage and dermal inflammation predominantly composed of neutrophils with occasional eosinophils. **B**, High-power view shows the inflammation and focal extravasated erythrocytes and leukocytoclasia and focal vascular wall damage. (**A** and **B**, hematoxylin-eosin stain; original magnifications: **A**, $\times 100$; **B**, $\times 200$.)

red blood cell casts. Repeat chest imaging found no evidence of thymoma recurrence.

Prednisone was increased to 60 mg/d, and dapsons (50 mg/d) was added with improvement in eruption and resolution of his arthralgia and microscopic hematuria. Methotrexate (20 mg/wk) was added as a second steroid-sparing agent with plans to taper the patient's prednisone.

COMMENT

Thymomas are frequently associated with autoimmune phenomena. Myasthenia gravis is the most common, and others include limbic encephalitis, neuromyotonia, and polymyositis, among many others.² The coincident onset of symptoms and diagnosis of thymoma in this patient raises high suspicion for a paraneoplastic etiology.

The most likely explanation for our patient's presentation is that he suffered 2 unique paraneoplastic

syndromes: urticaria and microscopic polyangiitis (MPA). The patient's rash at initial presentation had clinical features of urticaria, such as characteristic morphology, resolution within 24 hours without hyperpigmentation, and response to steroids, with supportive histopathology. In contrast, the rash that developed after thymectomy was clinically and histologically consistent with MPA, defined by the Chapel Hill Clinical Criteria as a small vessel necrotizing vasculitis without immune deposits.³ Antineutrophil cytoplasmic antibody–positive serologies are not necessary for the diagnosis of MPA, but the presence of pANCA with anti-myeloperoxidase specificity strongly supports the diagnosis. Other features consistent with MPA include the patient demographics (older age, white race), inflammatory arthritis, and the clinical progression from prodrome of constitutional symptoms to skin lesions and signs of kidney damage.

Our review of the literature found 1 previously reported case of MPA associated with thymoma. The patient was a 50-year-old white man whose presenting symptoms were arthralgias and skin eruption, similar to those of our patient. The skin findings were described as an “evanescent maculopapular rash” and did not undergo biopsy. Although thymectomy seems to have precipitated the onset of MPA in our patient, the previous case report describes severe exacerbation of MPA in the post-thymectomy setting. The patient’s disease course featured prominent renal and pulmonary manifestations of MPA, and there were no further skin findings.⁴

A second possible explanation is that MPA is the unifying diagnosis responsible for both the urticarial and the purpuric rash. This explanation would be consistent with the previously reported case of exacerbation of MPA in the post-thymectomy setting,⁴ as our patient’s condition also declined in the months after surgery. One theory to explain this phenomenon is immune dysregulation caused by imbalance of T-regulatory cells.

However, although cutaneous manifestations are present in about 50% of patients with MPA, our patient’s initial urticaria is not a characteristic finding. Urticaria has only to our knowledge been reported in 1 case, in which a 79-year-old man with pANCA-positive vasculitis had urticarial erythema. Biopsy of his lesions found neutrophils and fragmentation of nuclei in the dermal perivascular regions with negative immunofluorescence studies.⁵

The biopsy of our patient’s initial eruption did not show vasculitis, but steroid treatment could explain the lack of active vessel damage at that time.

A third explanation to consider is progression from common urticaria to urticarial vasculitis (UV). Hyperpigmentation and prolonged eruptions are typical of UV, and arthralgias and kidney damage are associated as well. UV can be associated with hypocomplementemia, and our patient had mildly decreased complement levels with the decrease corresponding to clinical progression. Hypocomplementemic UV is not typically associated with antineutrophil cytoplasmic antibodies.

Clinicians should be aware of the potential association of cutaneous vasculitis with thymoma and of the possibility that paraneoplastic eruptions may present after thymectomy.

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