SIGNIFICANCE STATEMENT

Pulmonary-renal syndromes, including Goodpasture syndrome (GP) and ANCA-associated vasculitis, are rapidly progressive glomerulonephritides. This study describes the discovery of an inhibitory anti-peroxidasin autoantibody within this disease spectrum that is present before and at the time of clinical GP presentation. *In vitro*, this antibody inhibited hypobromous acid production by peroxidasin, a critical step in the formation of sulfilimine crosslinks in the collagen IV autoantigen. Disruption of sulfilimine crosslinks is thought to expose the NC1 domain of collagen IV chains to recognition by autoantibodies in GP. The anti-peroxidasin antibodies are specific for peroxidasin but were also found in some patients with anti-myeloperoxidase ANCA vasculitis, and are associated with more active disease. Investigation of anti-peroxidasin antibodies may inform disease pathogenesis and better classification and prognostication in some patients.