In NEJM This Week: Vascular Complications of Rheumatic Diseases

By Norman Bauman [2]

Two case studies important to rheumatology, both reported by non-rheumatologists: Severe pulmonary hypertension comorbid with a connective tissue disorder, and Raynaud's that had progressed to digital necrosis.


Fazio S, A 34-Year-Old Woman with Increasing Dyspnea. Now@NEJM, March 21, 2014

This case study describes a 34-year-old woman with worsening shortness of breath diagnosed with severe pulmonary hypertension caused by mixed connective-tissue disorder.

When pulmonary hypertension is suspected, the initial diagnostic test is echocardiography. The confirmatory test is right heart catheterization, which gives more precise measurements and helps guide therapy. (This issue of N Engl J Med also has an unrelated Perspective, on the benefits of ultrasound diagnosis. (Point-of-Care Ultrasound in Medical Education — Stop Listening and Look).

One of the underlying causes of pulmonary hypertension is connective tissue disease. This patient had many nonspecific symptoms which, when taken together with test results (elevated inflammatory markers, a positive antinuclear antibody essay, and hypocomplementemia), suggest a collagen vascular disease. Those symptoms, all of which have been associated with connective-tissue diseases, include:

• symmetric pains in the knees, elbows, and hands that responded to glucorticoids,
• Raynaud’s phenomenon,
• dry mouth,
• abdominal pain,
• intermittent diarrhea,
• hair thinning,
• eczema,
• anemia, and
• benign axillary lymphadenopathy.

The differential diagnosis includes systemic lupus erythematosus (SLE) and scleroderma. This patient had features of both. The final diagnosis was mixed connective-tissue disease, an overlap syndrome with features of lupus, scleroderma, and polymyositis. (Some of these patients ultimately meet criteria for SLE or scleroderma.)

See also: Lung Disease in Scleroderma, Part I: Ten Points About ILD and Lung Disease in Scleroderma, Part II: Vital Basics About PAH

This patient had a positive test for the anti-U1-ribonucleoprotein antibody, a prerequisite for mixed connective tissue disease. Arthralgias, arthritis, swollen hands, Raynaud’s phenomenon, and pulmonary hypertension are prominent features. Treatment is given according to the disease that the patient's condition most closely resembles.

Mixed connective tissue disease has substantial morbidity and mortality. This patient’s right ventricular failure and severe pulmonary hypertension gave her a poor prognosis.

She was given continuous intravenous epoprostenol, followed by bosentan, sildenafil and treprostinil, which led to marked improvement. The mixed connective tissue disease was treated with hydroxychloroquine and prednisone, which also led to significant improvement.


Bilateral digital necrosis developed in a 69-year-old woman with a family history of Waldenström's macroglobulinemia and a diagnosis of Sjögren's syndrome with painful
Raynaud’s phenomenon.
Laboratory studies led to a diagnosis of cryoglobulinemia with IgM monoclonal gammopathy of unknown significance.
Treatment for the cryoglobulinemia with dexamethasone, cyclophosphamide, and rituximab, led to no improvement.
She was then treated with thoracic sympathectomy to increase perfusion, after which her hands became warm and moist. After one year, cryoglobulins were undetectable, the patient’s fingers had improved, and there were no amputations.