Granulomatosis and Polyangitis Followed by Alveolar Proteinosis in a 32-Year-Old Woman

To the Editor:

A 32-year-old white woman reported worsening dyspnea for 1 month without cough or fever. She had received a diagnosis of granulomatosis and polyangitis (GPA) 13 months previously, confirmed by kidney biopsy and an elevated serum antinuclear cytoplasmic antibody level. Her initial presentation of GPA included renal failure and alveolar hemorrhage with rash and arthralgias. At the time of our evaluation, she was dyspneic and hypoxemic with an oxygen saturation level of 86% on room air. She had bilateral diffuse rales without jugular venous distention, a cardiac gallop, rash, or synovitis. Her medications included 40 mg/d of prednisone and 75 mg/d of cyclophosphamide with double-strength trimethoprim-sulfamethoxazole 3 times weekly. She had not experienced a GPA recurrence previously. Her WBC count was 5,100 per μL with a hemoglobin count of 8.5 g/dL and a platelet count of 221,000 per μL.

A CT scan of the chest (Fig 1) revealed bilateral, diffuse ground-glass opacities. A subsequent bronchoscopy revealed a cloudy lavage that was negative for pathogenic infectious agents, including Pneumocystis jiroveci. There was no evidence of diffuse alveolar hemorrhage. Her antinuclear cytoplasmic antibody profile, erythrocyte sedimentation rate, and urinalysis results were normal. Lung function studies revealed an FVC of 2.70 L (74% predicted), a diffusing capacity of lung for carbon monoxide (Dlco) of 34% predicted, and a 6-min walk of 182 m with desaturation to 80% while receiving supplemental oxygen at 3 L/min by nasal cannula.

Despite increasing the prednisone to 60 mg/d and cyclophosphamide to 100 mg/d for a presumptive recurrence of her vasculitis as well as using empirical antimicrobial therapy for infection, her condition failed to improve. An open-lung biopsy revealed prominent alveolar accumulation of proteinaceous material that was positive using periodic acid-Schiff stain and focal accumulations of hemosiderin-laden macrophages without active vasculitis (Fig 2). A whole-lung lavage was attempted, but significant postoperative hypoxia and poor functional status allowed only a unilateral lavage. The lavage revealed opalescent, pink material that cleared by the completion of the procedure. Clinically, the patient continued to experience significant exertional dyspnea and hypoxemia. One week after the procedure, lung function studies revealed an FVC of 3.42 L (95% predicted), a Dlco of 70% predicted, and a 6-min walk of 337 m with a saturation of 97% on room air with walking. At a 6-month follow-up visit, the patient continued to be without dyspnea, cough, or exercise intolerance. Her lung function studies 9 months after presentation demonstrated an FVC of 3.66 L (102% predicted), a Dlco of 71% predicted, and a 6-min walk of 346 m.

We believe that active pulmonary disease in the patient was PAP rather than GPA, in that she failed to respond to immunosuppressive therapy directed toward GPA and antimicrobial therapy directed at suspected infection. In addition, her open-lung biopsy was diagnostic of PAP without concomitant evidence of GPA. The time course of her improvement correlated with the treatment of PAP using aerosolized GM-CSF. The acquired form of PAP is usually associated with autoantibodies to GM-CSF. The patient did not demonstrate autoantibodies on two separate occasions.

Because of the reported risk of subcutaneous GM-CSF in patients who are immunosuppressed and the suggestion of safety with the aerosolized form of GM-CSF in such patients, we initiated the use of aerosolized GM-CSF with 250 μg bid Leukine (Immunex Corporation): 1 week on and 1 week off for 3 months. A chest CT scan 4 weeks after starting this therapy showed complete resolution of the ground-glass opacities. Lung function studies revealed an FVC of 3.42 L (95% predicted), a Dlco of 70% predicted, and a 6-min walk of 337 m with a saturation of 97% on room air with walking.
sustaining that the PAP may have been a secondary event and not antibody mediated. The exact mechanism is unknown. Other secondary causes of PAP include hematologic malignancy and dust exposure. In summary, we present a patient with GPA followed by PAP, effectively treated using aerosolized GM-CSF.

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Financial/nonfinancial disclosures: The authors have reported to CHEST the following conflicts of interest: Dr Judson has received grant support from Celgene Corporation over the past 3 years. He is a consultant for Centocor and Pulmonary Reviews. He is on a speakers bureau for Pfizer and Boehringer Ingelheim. Drs Compa and Beegle have reported that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

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DOI: 10.1378/chest.11-2002

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Interstitial Lung Disease and Antinuclear Antibody

Consider Nonspecific Interstitial Pneumonia Histology and Newer Antibodies

To the Editor:

The recent article by Vij et al. in CHEST (November 2011) on autoimmune-featured interstitial lung disease (AIF-ILD) raises some further interesting questions. It is well described that connective tissue disease-related interstitial lung disease often is associated with nonspecific interstitial pneumonia (NSIP) histologic test results.1 Intuitively, those patients with AIF-ILD might be expected to have a higher chance of underlying connective tissue disease and, thereby, NSIP on histologic testing and a better prognosis compared with those patients who have standard interstitial lung disease and usual interstitial pneumonia histologic results. It is noted in the study that only a small proportion had NSIP histologic results, and the greater majority had usual interstitial pneumonia histologic results in the AIF-ILD group. Those with a higher antinuclear antibody (ANA) titer level had a better prognosis.

One would postulate a higher prevalence of NSIP and atypical radiologic results in cases associated with a better prognosis. From the article, it seems from the 17 patients with higher titer ANA levels mentioned, there was a higher proportion with NSIP histologic results (20% of patients who receive biopsies vs 6% overall) and slightly higher proportion with atypical radiologic results (38% vs 33% overall) associated with better survival.

Newer antibodies are being detected with time (for example, myositis-specific antibodies1-4), and current autoantibody panels may not detect all antibodies. Therefore, could it be possible that those with a higher ANA titer level or NSIP histologic results (portending a better prognosis) might have additional, more specific, but as yet undetected antibodies?

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Financial/nonfinancial disclosures: The author has reported to CHEST that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

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DOI: 10.1378/chest.11-3116

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