suggesting 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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REFERENCES

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 antibodies3-4), 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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Response

To the Editor:

We thank Dr Medford for his insightful comments regarding our study evaluating the characteristics and survival of patients with autoimmune-featured interstitial lung disease (AIF-ILD). These patients had signs or symptoms and serologic test results suggestive of autoimmunity but did not meet the criteria for a defined connective tissue disease. Although survival for all patients with AIF-ILD was comparable to patients with idiopathic pulmonary fibrosis, the subgroup of patients with AIF-ILD and an antinuclear antibody (ANA) titer \( \geq 1:1280 \) had improved survival. As Dr Medford noted, nonspecific interstitial pneumonia patterns, which are generally associated with improved outcomes, were seen more commonly in the subgroup of patients with AIF-ILD and an antinuclear antibody (ANA) titer \( \geq 1:1280 \) had improved survival. As Dr Medford noted, nonspecific interstitial pneumonia patterns, which are generally associated with improved outcomes, were seen more commonly in the subgroup of patients with AIF-ILD and high ANA titers. Nonetheless, the majority of patients with AIF-ILD and high ANA titers had a usual interstitial pneumonia pattern on CT scan and lung biopsy (59% and 73%, respectively), suggesting that radiographic and histopathologic patterns may not fully account for the differences in survival. The small number of patients with AIF-ILD and high ANA titers precluded subgroup analysis to determine the impact of radiographic and histopathologic patterns on survival. Our results underscore the significance of performing a systematic evaluation for autoimmune features in patients with interstitial lung disease regardless of radiographic and pathologic patterns, as patients with usual interstitial pneumonia may meet the criteria for AIF-ILD. More importantly, the presence of elevated ANA titers may have prognostic value.

Evaluation for underlying autoimmune disease may evolve as newer autoantibodies are discovered, as in the case of the anti-synthetase syndrome. As Dr Medford suggests, this may also be true for patients with AIF-ILD and high ANA titers. Until then, we believe that it is crucial to evaluate for and recognize the subgroup of patients with AIF-ILD so that additional studies of their disease course, predictors of survival, and response to therapy can be performed.

We hypothesize that there is a spectrum of autoimmunity in interstitial lung disease and that the presence of autoimmunity may impact both response to treatment and survival. Current diagnostic criteria for AIF-ILD rely on clinical characteristics, some of which are nonspecific. As a result, AIF-ILD encompasses a heterogeneous group of patients: Some may have a clinical course similar to patients with idiopathic pulmonary fibrosis, while others may have a course similar to patients with connective tissue diseases. Additional studies of the molecular differences related to autoimmunity for patients with interstitial lung diseases may lead to the development of additional criteria that can be used to objectively distinguish between these subgroups of patients.

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Sepsis, Lactate, and Oxygen Supply Dependence

To the Editor:

I read with great interest the Point/Counterpoint Editorials of Jones and Rivers et al in CHEST (December 2011). A central supposition of both, however, is that sepsis/septic shock is a condition in which oxygen consumption is dependent on oxygen delivery (Do\(_{2}\)). Studies suggesting such were discounted in the 1990s as (measurement) artifact of mathematical coupling. Although nitric oxide–mediated microvascular dysregulation is certainly a feature of septic shock, data are not so conclusive that tissue-level Do\(_{2}\)/oxygen consumption mismatch contributes to tissue hypoxia/hyperoxia or lactic acidosis (LA). Nobody would argue that patients with severe hypotension during septic shock may have some LA resulting from hypoxia (when/if extraction fractions exceed around 60%); but LA often persists after resuscitation. And both debaters agree that generation of LA in sepsis is complex, if not completely understood.