AE-IPF, and it could be argued (and is possible) that acute exacerbations of IPF may also represent some unidentified infectious trigger.

In conclusion, we propose that the clinical course of fibrotic HP, like other forms of fibrotic lung disease, can be associated with idiopathic AEs of disease leading to rapid respiratory deterioration and predicting a poor outcome. Further investigations into the similarities between these fibrotic lung diseases and the (possible) common pathway of AEs may yield additional insights into this recently recognized syndrome and, possibly, a better understanding of the mechanisms of fibrosis involved in these different disease processes.

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Etanercept-Induced Lupus Erythematosus Presenting as a Unilateral Pleural Effusion*

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A 72-year-old man receiving etanercept for the treatment of psoriatic arthritis had an exudative pleural effusion with nonspecific fluid analysis and pleural biopsy findings. He was ultimately found to have drug-induced lupus erythematosus due to the etanercept. The spectrum of autoimmune disease due to the use of tumor necrosis factor inhibitors is reviewed. ***(CHEST 2008; 134:850–853)***

Key words: etanercept; lupus erythematosus; pleural effusion; tumor necrosis factor

Abbreviations: ANA = anti-nuclear antibody; RA = rheumatoid arthritis; SLE = systemic lupus erythematosus; TNF = tumor necrosis factor

A 72 -year-old man with psoriatic arthritis who had been treated with etanercept, 50 mg, subcutaneous injection weekly and prednisone (that had been slowly tapered, down to 1 mg every other day at the time of presentation) had pleuritic chest pain with dyspnea and dry cough that progressed over several weeks. He had a 50-pack-year smoking history. He denied exposure to asbestos.

The patient was afebrile and had normal vital signs. The chest examination was remarkable for dullness to percussion and reduced breath sounds on the left. Psoriatic plaques were noted throughout the extremities, and he had no signs of active arthritis. His hemoglobin level was 13.3 g/dL; leukocyte count was 9,900/μL; albumin was 2.6 g/dL; total protein was 6.4 g/dL; BUN was 7 g/dL; and creatinine was 0.7 g/dL. Radiologic examination confirmed the presence of a large left-sided pleural effusion (Fig 1, *top*). Thoracentesis was performed, and pleural fluid analysis revealed an exudative effusion, with a pH of 7.5, glucose of 79 mg/dL, lactate dehydrogenase of 210 IU/L (serum lactate dehydrogenase was 148 IU/L), and total protein of 4.3 g/dL. The fluid contained 909 WBCs/μL, with 100% of the cells being mononuclear. Microbiological and cytologic evaluations of sputum and pleural fluid were negative.

Given the uncertainty of the diagnosis, the patient underwent video-assisted thoracoscopic pleural and lung biopsy. The pleura was markedly thickened, with an acute and chronic inflammatory cell infiltration. Lymphocytes formed occasional lymphoid nodules, and there were a large number of plasma cells (Fig 2). Rare small arterioles demonstrated fibrinoid necrosis of the media, a finding characteristic of lupus erythematosus.(Fig 2, inset). The lung parenchyma near the pleura demonstrated some inflammation, but the parenchyma away from the pleura was unremarkable.

Subsequently, anti-nuclear antibody (ANA) returned positive in a homogeneous pattern, with a titer of 1:2560. Anti-histone antibodies returned at 8.5 U (normal range < 1.0 U). He had never been tested for ANA previously. Based on the above findings, a diagnosis of drug-induced lupus was made, attributed to the use of etanercept. Prior to withdrawal of the etanercept, he had partial recurrence of his left pleural effusion, with concomitant development of right pleural abnormalities (Fig 1, *center*). Six weeks after withdrawal of the etanercept and a brief taper of prednisone starting at 30 mg/d, a repeat chest radiograph

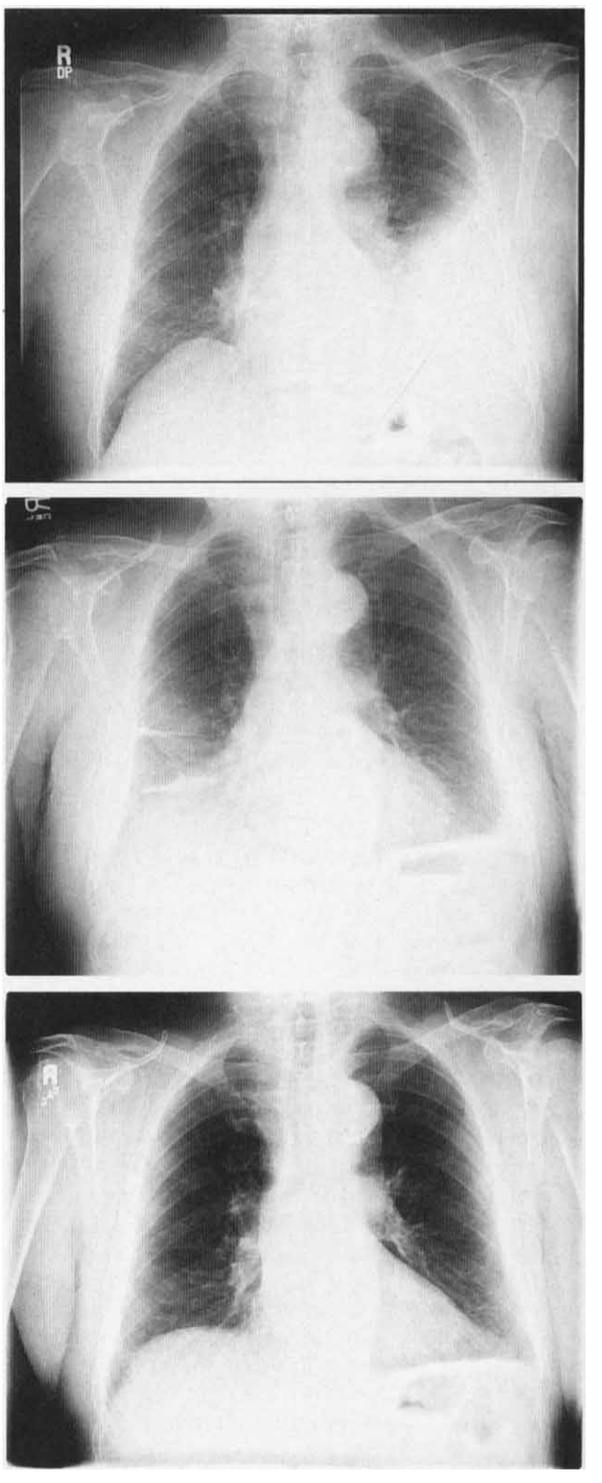

FIGURE 1. *Top*: Posteroanterior chest radiograph demonstrating a large left pleural effusion without obvious parenchymal abnormalities. *Center*: Posteroanterior chest radiograph demonstrating a left pleural effusion with new right pleural thickening and/or effusion. *Bottom*: Posteroanterior chest radiograph demonstrating near-complete resolution of the bilateral pleural abnormalities.

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