lack of acute bronchiolitis with surrounding interstitial pneumonia in materials from biopsy argue against the diagnosis of pneumonia due to *Mycoplasma pneumoniae*. The organisms illustrated in Figure 3 are definitely not *Mycoplasma*, which is elongated and filamentous and possesses a hook-like terminal structure.

Although the presence of abnormal results on tests of pulmonary function might be due in part to preexisting obstructive pulmonary disease, the patient was active and had no dyspnea prior to this illness. A chest roentgenogram taken two years earlier was essentially normal, except for mild blunting of the left costophrenic angle.

This case illustrates that at least some patients with Legionnaires' disease may be left with long-term residual damage. Careful follow-up of other known survivors will be needed to clarify this important point.

**References**


**Apical Fibrobulous Disease with Rheumatoid Arthritis**

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We describe a patient who developed noninfectious apical fibrobulous disease 12 years after the diagnosis of seropositive, nodular, deforming rheumatoid arthritis. Fibrobulous disease of the pulmonary apices is a rare entity that is usually found in association with ankylosing spondylitis. Its appearance with rheumatoid arthritis has not been reported. Speculative factors which may predispose to apical fibrobulous disease, such as a stiff chest wall, impaired esophageal motility, and HL-A antigen B27, were not present in our patient.

In the absence of neoplasia, fungal disease, or tuberculosis, apical fibrobulous disease is a rare disorder. There is sporadic occurrence of the disease; however, apical fibrobulous changes are primarily found in association with ankylosing spondylitis.1,2 This association has fostered speculation concerning the mechanism of this disorder in a disease which is characterized by a stiff chest wall, abnormal esophageal motility, and the marker of HL-A antigen B27. To our knowledge, apical fibrobulous disease has been reported with only the rheumatic diseases of ankylosing spondylitis and Reiter's syndrome.3 The purpose of this report is to describe a patient with rheumatoid arthritis who developed progressive bilateral apical fibrobulous changes and to discuss the previously proposed pathophysiologic mechanisms of the apical changes.

**Case Report**

A 42-year-old man was referred for evaluation of hemoptysis. Twelve years prior to admission, the diagnosis of rheumatoid arthritis had been made on the basis of several deformities of peripheral joints, subcutaneous nodules, and a positive latex-fixation test. Two and one-half years prior to admission, a chest roentgenogram had shown bilateral bulous disease in the apices and an interstitial pattern at both bases (Fig 1).

Eight months prior to admission, the patient had been evaluated for cavitation of the right upper lobe. Multiple cultures of sputum for tuberculosis and fungi were negative. Since then, the patient had noticed a daily cough, with production of sputum and occasional hemoptysis. He denied fever, sweats, malaise, and loss of weight. The arthritis has been controlled with daily therapy with aspirin. A total

**Figure 1.** Chest roentgenogram 2½ years prior to admission.
replacement of the right knee had been performed six years previously. Four years prior to admission, a barium swallow and upper gastrointestinal radiographic study had been performed for evaluation of episodic dyspepsia; the results were normal. The patient had smoked one pack of cigarettes daily for 27 years.

On physical examination, the patient had severe deformities of the peripheral joints and subcutaneous nodules over the extensor surfaces of both forearms. The vital signs were normal. Examination of the chest revealed dullness to percussion over the right upper posterior pulmonary fields. Breath sounds were slightly diminished in the same area. There were no adventitial breath sounds. Cardiac examination revealed no murmurs or gallop rhythms. The findings from examination of the abdomen were unremarkable. The extremities showed clubbing of all digits.

Laboratory studies disclosed normal values for the following: hematocrit reading; serum levels of electrolytes; chemical constituents of the serum; white blood cell count; and differential cell count. The latex-fixation titer was 1:80. Antinuclear antibody and HL-A antigen B27 were absent. The level of α₁-anti-trypsin was above the normal range. A chest roentgenogram showed fibro-bullous changes at both apices, which were more prominent on the right, with a normal cardiac size (Fig 2). X-ray films of the hands disclosed the changes of severe rheumatoid arthritis. Arterial blood gas levels included a pH of 7.36, an arterial oxygen pressure of 81 mm Hg, and an arterial carbon dioxide tension of 40 mm Hg. Tests of pulmonary function disclosed a forced vital capacity (FVC) of 4.25 L (84 percent of predicted), a forced expiratory volume in one second (FEV₁) of 2.55 L (66 percent of predicted), a ratio of FEV₁/FVC of 60 percent (predicted normal, 76 percent), a residual volume of 1.74 L (87 percent of predicted), and a total lung capacity of 5.90 L (85 percent of predicted).

Cutaneous testing with intermediate-strength purified protein derivative of tuberculin was negative. Fiberoptic bronchoscopy examination revealed a normal tracheobronchial tree. Bronchial washings disclosed no acid-fast bacilli, and cultures showed no growth for tuberculosis or fungi. The findings from cytologic examination were unremarkable. Complement-fixation tests for Histoplasma capsulatum, Blastomyces dermatitidis, Aspergillus fumigatus, and Coccioides immitis were negative. The patient has been followed-up with biannual chest roentgenograms. No further studies are planned unless the patient develops significant hemoptysis.

FIGURE 2. Chest roentgenogram on admission.

DISCUSSION

This patient exhibits classic rheumatoid arthritis with a positive latex-fixation titer. Twelve years after the diagnosis of rheumatoid arthritis, he developed cough and hemoptysis and was found to have apical fibro-bullous changes on the chest roentgenogram that were unexplained by tuberculosis, fungal disease, or neoplasia. It is unlikely that these findings represent a breakdown of rheumatoid nodules, as has been described by Matthay et al, since sequential chest roentgenograms revealed progressive bullous changes followed by fibrosis in the upper lobes. Furthermore, at no time has a nodular pattern been present on the chest roentgenogram.

Several mechanisms have been proposed to explain apical fibro-bullous disease, and all depend heavily on its association with ankylosing spondylitis. Abnormal esophageal motility has been found in some patients with ankylosing spondylitis and aspergillomas in the upper lobes. It has been suggested that impaired esophageal motility may predispose to chronic aspiration, with resultant fibrosis and colonization of the tracheobronchial tree by aspergillus. Our patient has no symptoms of regurgitation or aspiration, and the findings from gastrointestinal studies for dyspepsia were unremarkable. Moreover, an association between rheumatoid arthritis and abnormal esophageal motility or chronic aspiration has not been demonstrated.

Another proposed mechanism implicates the stiff chest wall found in patients with ankylosing spondylitis. It has been demonstrated that such patients have decreased perfusion and ventilation of the apices, probably because of poor movement of the chest wall and primarily diaphragmatic breathing. The postulate is that this may lead to bullous changes and fibrosis in the apices by some unknown mechanism; however, our patient with rheumatoid arthritis showed normal thoracic excursion on physical examination and had no ankylosis of his costovertebral joints by radiologic examination.

A third proposal is based upon the strong association of HL-A antigen B27 with ankylosing spondylitis. Data are scant. From the literature, four of nine patients with ankylosing spondylitis and one of two patients with Reiter’s syndrome have demonstrated positive markers and apical changes. Our patient with rheumatoid arthritis, as expected, had no HL-A antigen B27; however, it is highly possible that apical fibro-bullous disease is linked with individual or disease-related immunologic mechanisms.

ACKNOWLEDGMENTS: We are grateful to Dr. P. Khavari for the referral of this patient and to Drs. M. J. Hensley and N. A. Saunders for their critical review of the manuscript.

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Resin Hemoperfusion as Treatment for Theophylline-induced Seizures*


Hemoperfusion with resin was used to treat a 63-year-old man with seizures secondary to theophylline intoxication. The patient illustrates the efficacy of treatment by resin hemoperfusion in this situation, emphasizes the risk of fixed theophylline dosage regimens and the necessity of monitoring plasma theophylline concentrations in acutely ill patients.

Theophylline has a narrow but well-defined therapeutic range (10-20 µg/ml) and as drug concentrations exceed this range, dangerous side-effects occur in the form of cardiac arrhythmias and seizure activity. These side-effects may be refractory to conventional therapy and carry a high mortality. Optimal administration of theophylline is complicated by large intersubject and intrasubject variability in theophylline clearance. Liver disease, heart failure, age, and high carbohydrate-low protein diet may all prolong theophylline clearance and predispose to toxicity. Hemodialysis, and more recently resin hemoperfusion, have been utilized in the aggressive management of theophylline toxicity.

CASE REPORT

A 63-year-old white man weighing 69 kg was hospitalized because of progressive dyspnea and ankle swelling. He was a heavy smoker, and had smoked 25 cigarettes a day for the previous 50 years; he gave a history of episodic wheezing and productive cough for many years. There was no history of previous seizures, liver disease or excessive alcohol intake and he was taking no medication. Physical findings on admission included marked expiratory wheezing, signs of right heart failure, but no hepatomegaly or other signs of hepatic dysfunction. Routine liver function studies were all within the normal range.

Treatment was instituted with controlled oxygen therapy and intravenous amphetamines, 0 mg/kg as a loading dose over 30 minutes and then 0.9 mg/kg/hour as an intravenous maintenance infusion. Despite these measures, the patient continued to deteriorate and required mechanical ventilation on his third day in the hospital. Seven days after admission, he developed ventricular premature beats and, after two grand mal seizures, went into status epilepticus which was refractory to large doses of intravenous diazepam and phenytoin. The aminophylline infusion was discontinued immediately and a plasma theophylline concentration obtained two hours later was 40.5 µg/ml. Because of the risk of continuing seizure activity and malignant cardiac arrhythmia, renal hemoperfusion was instituted.

Hemoperfusion was accomplished by placing a Sheldon catheter in the left femoral vein to provide input to the Amberlite column at 300 ml/min, and return was through the left subclavian vein. Blood was drawn half-hourly from the input line for the 24 hour duration of hemoperfusion and then at regular intervals during the 36 hours following the hemoperfusion. No adverse effects were noted from the period of hemoperfusion and the seizure activity abated during this period. Phenytoin plasma concentrations were determined using an enzyme immunoassay (EMIT), and theophylline plasma concentrations were measured using a high pressure liquid chromatographic assay. Protein binding of 14C theophylline was assessed at a pH of 7.4 at a theophylline concentration of 15 µg/ml by equilibrium dialysis.

The theophylline and phenytoin plasma concentrations are shown in Figure 1. During the 24 hour hemoperfusion, theophylline concentrations fell from 36.6 µg/ml to 14.1 µg/ml and phenytoin concentrations from 18.5 µg/ml to 10.2 µg/ml. Theophylline plasma concentrations before and after hemoperfusion are plotted logarithmically against time and the plasma half-life (t½) derived from the slope of the elimination phase which was assessed by the method of least squares. The t½ prior to hemoperfusion was 19.6 hours and after hemoperfusion 13.3 hours. In our patient, 33 percent of theophylline was protein bound compared to that of six age-matched normal subjects 46 percent ± 2.5 (mean ± SD).

DISCUSSION

The dosage of theophylline our patient received was in line with standard recommendations for the use of intravenous theophylline. These dosage guidelines more recently have been felt to be too rigid and not to take account of the effects of age and associated illnesses on theophylline metabolism. The theophylline disposition in our patient was difficult to predict as smoking increases theophylline clearance, whereas heart failure decreases it. This report emphasizes the necessity for monitoring theophylline plasma concentrations for safe and effective therapy. It is important that this monitoring be continued for the total duration of therapy, as a large intrasubject variability of theophylline clearance has been observed over a four-day period in acutely ill patients. It should also be noted that our patient was

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CHEST: 75: 6, JUNE, 1979