Hypoxemia with Normal Chest Roentgenogram due to Pneumocystis carinii Pneumonia*

Diagnostic Errors Due to Low Suspicion of AIDS

Harold L. Israel, M.D.; Jonathan E. Gottlieb, M.D., F.C.C.P.; and Edward S. Schulman, M.D., F.C.C.P.

Three patients encountered in a single month had insidious development of atypical respiratory or systemic symptoms and were found to be hypoxic. All had normal chest roentgenograms and were perplexing problems in diagnosis. On initial presentation, none had evidence of pulmonary infection or recognized clinical or social features that suggested acquired immunodeficiency syndrome (AIDS). All received corticosteroids for respiratory distress before the correct diagnosis was made, and all died rapidly of Pneumocystis pneumonia secondary to AIDS.

Hypoxemia, as the dominant manifestation in patients with normal chest roentgenogram findings is uncommon and usually results in investigation for pulmonary embolism or for diffuse interstitial fibrosis which may occasionally present in this fashion.

This unusual constellation was encountered in a single month in three patients whose onset provided no intimation of serious pulmonary infection, and whose social and clinical appearances offered no suggestion of the acquired immune deficiency syndrome (AIDS). All three patients received corticosteroid therapy before the correct diagnosis was established and all died of respiratory failure within three months of onset of symptoms.

Case Reports

Case 1

A 35-year-old married black male office worker with two children sought medical attention early in June 1986 because of cough for four weeks and dyspnea on exertion for a week; he denied homosexual encounters. He was in a suburban hospital for three days where a chest physician instituted treatment with bronchodilators and prednisone with temporary relief. He was readmitted three days after discharge because of growing distress and was found to have a PaO2 of 55 mm Hg while breathing room air. Chest x-ray film, perfusion-ventilation, and gallium scans were normal. His oxygen tension deteriorated despite treatment with erythromycin and increased doses of prednisone. On transfer to the Thomas Jefferson University Hospital on July 8, 1986, the PaO2 was 55 mm Hg, and the chest roentgenogram remained clear. The forced vital capacity was 2.08 L (48 percent of predicted) with an FEV1 of 1.72 L. The diffusing capacity for carbon monoxide was 30 percent of predicted. Fiberoptic bronchoscopy was performed July 11 with transbronchial biopsies showing mild interstitial inflammation and negative stains for Pneumocystis, acid-fast organisms, and fungi. Lavage was not performed because of incessant coughing despite 400 mg of lidocaine. Respiratory failure became increasingly severe, and diffuse alveolar infiltrates appeared on the chest roentgenogram of July 17. Open lung biopsy, July 18, revealed large numbers of Pneumocystis. An ELISA assay for HIV antibody was positive. When informed of the diagnosis, the patient admitted to occasional homosexual relations. Therapy with intravenous sulfamethoxazole-trimethoprim followed by pentamidine was unavailing, and the patient died of respiratory and renal failure on Aug 9, 1986.

Case 2

A 68-year-old black widow had noted anorexia, night sweats, vomiting, and 6.8 kg (15 pound) weight loss over a period of weeks culminating in a syncopal episode on July 29, 1986. Chest x-ray film findings in the Emergency Ward (Fig 1, upper) and electrolyte values were normal. The hemoglobin was 9.1 g, and white blood cell count, 4,200, with normal differential. She was admitted to the general medical service where arterial blood gas study disclosed pH of 7.38, PaO2 of 52 mm Hg, PaCO2 of 31 mm Hg, and an oxygen saturation of 87 percent. The oxygen tension quickly became normal on administration of oxygen by nasal catheter. She subsequently underwent extensive investigation in a search for an occult neoplasm. After cardiac, gastroenterologic, endocrinologic, and neurologic studies proved fruitless, attention turned to the persistent hypoxemia. On August 7, she had a second syncopal episode, and for the first time, was noted to be dyspneic. A ventilation-perfusion lung scan was ordered. The perfusion scan was normal, but on completion of the test, she became pulseless, and was resuscitated and intubated. On transfer to the Respiratory Intensive Care Unit, x-ray examination showed bilateral pulmonary edema. (Fig 1, lower) and the arterial oxygen tension was 30 mm Hg. Leukens aspirates revealed no pathogens, and she was treated for acute respiratory distress syndrome of uncertain cause. On August 13, bronchoscopic examination was performed but bronchialalveolar lavage findings were negative while bronchial brushings were positive for Pneumocystis carinii. An ELISA assay for HIV antibody was positive. Treatment with intravenous sulfamethoxazole-trimethoprim was instituted with slight clearing of the roentgenographic densities but with no significant improvement in respiratory failure. The patient died on September 5.

*From the Division of Pulmonary Diseases, Department of Medicine, Jefferson Medical College, Thomas Jefferson University, Philadelphia.

Manuscript received February 9, revision accepted April 9.

Reprint requests: Dr. Israel, Jefferson Medical College, Philadelphia 19107

CHEST 92 5 NOVEMBER, 1987 857
Hypoxemia with Normal Chest Roentgenogram in PC Pneumonia (Israel, Gottlieb, Schulman)

**CASE 2**

The patient had undergone coronary artery bypass surgery in March 1982, at which time she received 4 units of frozen plasma, 1 unit of whole blood, and 6 units of packed red blood cells. She was readmitted in July 1982 and was found to have non-A- non-B hepatitis attributed to the transfused blood. During a third hospitalization in March 1985 for subendocardial myocardial infarction, she received 3 units of packed red blood cells because of anemia. She had had no further difficulties with angina, but she was hospitalized again from January 7 to February 4, 1986, because of severe herpes zoster of the left trigeminal area, treated with acyclovir and prednisone. No further corticosteroid therapy was given until admission to the Respiratory Intensive Care Unit where she received 400 mg hydrocortisone daily from August 8 to 10.

**CASE 3**

A 75-year-old white woman was seen in office consultation on July 7, 1986, because of cough and dyspnea gradually increasing over the past six weeks. She had been hospitalized for acute myocardial infarction in 1975, and had resection of abdominal aortic and iliac aneurysms with Dacron graft replacement on May 1, 1984. Following this procedure, she developed widespread psoriasis which had increased in severity despite outpatient therapy.

Hypoxemia was noted on evaluation in the office. A chest roentgenogram performed on July 30, 1986, showed a new area of consolidation in the right upper lobe. Blood cultures from the chest x-ray yielded Enterococcus faecalis. Despite continued antibiotics, arterial oxygen levels did not improve, and on September 10, open lung biopsy was performed. Large numbers of Pneumocystis cysts were seen on silver stain, and cytomegalovirus was demonstrated on culture. Subsequent studies included a positive HIV antibody. Treatment with intravenous sulfamethoxazole-trimethoprim was instituted without response. The patient died of respiratory failure on Sept. 22, 1986.

**DISCUSSION**

All three patients appeared unlikely candidates for contraction of AIDS, and its presence in each instance was not considered until P carinii pneumonitis was discovered. The initial chest roentgenogram was in each case entirely free of pulmonary disease (Fig 1, upper). Normal chest roentgenogram findings in patients known to have Pneumocystis pneumonitis and AIDS is infrequent. In one study, only three of 92 patients with pulmonary involvement due to AIDS had totally normal chest films, and only one of 22 patients examined had a normal gallium scan; in another study, normal chest roentgenograms were found in five of 81 patients. Pulmonary function tests in the two patients studied showed moderate reduction in lung volumes with marked reduction in diffusing capacity. Gallium-67 scans were performed in two patients. It is noteworthy that the normal scan in case 1 was performed after prednisone therapy had been started; this probably suppressed uptake. In case 3, a gallium scan showed 3+ diffuse bilateral lung uptake. Tuberculin tests and recall antigens were negative in all three patients.
patients. Antibodies to HIV virus were present in high titers in each case. No other abnormal laboratory test results were noted except for progressive anemia and rapid sedimentation rates.

Alveolar and interstitial infiltrates appeared in chest roentgenograms taken two to eight weeks after hospitalization and exhibited little response to either corticosteroid or antibiotic therapy. No significant clinical response to therapy for Pneumocystis was observed. Death occurred five, six, and ten weeks after initial hospitalization.

The failure to detect Pneumocystis on bronchoscopic examination in case 1 and 3 is unusual and may reflect a smaller number of organisms in pulmonary lesions too small to be detected on the chest roentgenogram. The absence of response to drug therapy and rapidly fatal course in the three patients may be due to the advanced age of two patients; although the inappropriate corticosteroid therapy may not have affected the ultimate outcome, its use was unwise. The cases we have described re-emphasize the necessity for caution in treating respiratory distress of uncertain cause with corticosteroids.

Since screening for HIV antibodies was instituted in May 1985 at Thomas Jefferson University Hospital, HIV antibodies have been found among donors at a rate of three per thousand. The development of AIDS in our two patients, one who received 13 units and the other 10 units, supports recent recommendations for serologic testing of all patients who received transfusions between 1979 and 1985.

The three cases reported emphasize the necessity of considering Pneumocystis pneumonia and AIDS in patients with unexplained hypoxemia even when the roentgenographic and gallium scan changes usually encountered are absent.

REFERENCES
1 Hopewell RC, Luce JM. Pulmonary involvement in the acquired immunodeficiency syndrome. Chest 1985; 87:104-12