**Bilateral Tuberculous Pleural Effusions With Markedly Different Characteristics**

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A 72-year-old man presented with malaise, weight loss, and cough. Chest radiograph revealed bilateral pleural effusions. On thoracentesis, the left effusion was a clear yellow exudate with more than 90% lymphocytes, and the right effusion was a grossly bloody exudate with more than 90% neutrophils. Cultures of both effusions grew *Mycobacterium tuberculosis*.

(CHEST 1996; 110:849-50)

**Key words:** elderly; pleura; tuberculous

**Abbreviations:** AFB=acid-fast bacilli; LDH=lactate dehydrogenase; PMN=polymorphonuclear leukocyte; PPD=purified protein derivative; TB=tuberculosis

*Mycobacterium tuberculosis* remains a pathogen of considerable clinical and public health importance. Classically, tuberculous pleuritis was regarded as a disease of young adults characterized by a unilateral, lymphocytic exudate with a self-limited short-term course. In the last two decades, however, there has been increasing recognition that tuberculous pleuritis is occurring in an older patient population, with reaction as well as primary disease, and that its features often vary from this classic picture. We report the case of an elderly man with bilateral tuberculous pleural effusions—one lymphocytic and the other persistently neutrophilic.

**Case Report**

A 72-year-old black man presented to the Hospital of St. Raphael with complaints of malaise, weight loss, shortness of breath, and minimally productive cough. His symptoms were present for 3 months, but had recently worsened. He was an alcoholic but had no significant medical history. He was a nonsmoker with no clear history of asbestos exposure, although he had worked as a custodian. There was no history of tuberculosis (TB), TB exposure, or purified protein derivative (PPD) skin testing.

On physical examination, his temperature was 38.6°C, pulse rate was 130 beats per minute, respirations were 40 breaths per minute, and BP was 103/80 mm Hg. There was no adenopathy. Lung examination revealed dullness to percussion and absent breath sounds at the bases. There was no hepatosplenomegaly, and no clubbing, cyanosis, or edema of the extremities. Results of neurologic examination were normal except for mild confusion. Hemoglobin and WBC count were normal at 15.3 g/dL and 6.3×10³/mL, respectively. Chest radiograph showed bilateral pleural effusions, the right loculated, and a small right upper lobe parenchymal density (Fig 1). Thoracentesis of the left effusion revealed clear yellow fluid with a pH of 7.27, protein level of 6.4 g/dL, lactate dehydrogenase (LDH) level of 348 IU, and glucose level of 65 mg/dL. There were 2,500 WBCs per cubic millimeter (92% lymphocytes, 5% polymorphonuclear leukocytes [PMNs], and 3% mononuclear cells). Gram and acid-fast bacilli (AFB) stains were negative. Therapy was started for bacterial pneumonia, and a 5-tuberculin-units PPD skin test was placed. On the third hospital day, a right thoracentesis was performed. The fluid was maroon colored and had a pH of 7.0, protein level of 7.2 g/dL, LDH level of 2,544 IU, and glucose level of 15 mg/dL. WBC count was 5,200/mm³ (90% PMNs, 3% lymphocytes, 7% mononuclear cells). Gram's stain and AFB smears were again negative. Chest tube drainage was not initiated, despite the low pH and elevated LDH level, because we were not convinced the effusion was parapneumonic.

The PPD skin test demonstrated 25 mm of induration at 72 h. The patient remained febrile despite antibacterial therapy and TB was strongly suspected. Repeated bilateral thoracenteses showed the cell counts and chemistry values on both effusions unchanged. Bacterial cultures of the blood and pleural fluid were all negative. Needle biopsy of the right pleura performed on the seventh hospital day revealed only mild chronic inflammation; no granulomas or AFB were seen. Five sputum specimens, urine, gastric aspirate, cerebrospinal fluid, and bronchial washings were also smear negative for AFB. We allowed ourselves to be dissuaded from the diagnosis of TB. On the 21st hospital day, thoracoscopic right pleural biopsy was done. Pleural fluid showed a persistent neutrophilia (89% PMNs). Histopathologic examination again revealed only inflammation, without granulomata or AFB.

The patient's course was complicated by nosocomial pneumonia, respiratory failure, and hemodynamic instability. On hospital day 28, cultures of both the right and the left effusions were reported to be growing *M tuberculosis*. Subsequently a second culture from each side and the needle biopsy specimen of the right pleura all grew *M tuberculosis*. The patient was placed on a multidrug regimen of antituberculous chemotherapy, his condition slowly improved, and he was discharged from the hospital to a long-term care facility.

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Manuscript received January 16, 1996; revision accepted March 14.

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Figure 1. Hospital admission chest radiograph demonstrating bilateral pleural effusions, the left loculated, and a small right upper lung zone parenchymal abnormality.
DISCUSSION

The classic teaching that tuberculous pleurisy is a disease of the young characterized by a unilateral exudate, occurring shortly after primary infection and unaccompanied by clinical parenchymal disease, is no longer valid. Increasingly, TB is being seen in an older patient population and its manifestations in this population differ.

In the review by Sibley1 of 200 cases of tuberculous pleurisy published in 1950, the mean age of the patients was 20 years. Subsequent series have shown a progressively higher proportion of older patients as well as a rise in the frequency of coexisting pulmonary parenchymal disease. Less than 25 years after Sibley’s report, Berger and Mejia2 published their experience with 49 patients with tuberculous pleurisy. Half of their patients were older than 55 years. 81% were older than 40 years, and 37% had coexisting parenchymal disease. Similarly, in the review by Epstein and colleagues3 of 26 patients with tuberculous effusions seen between 1978 and 1985, the median age was 56 years, with 19% of the cases occurring in the setting of reactivation disease. Fully 13% of their patients had bilateral pleural disease, as was seen in our patient, a manifestation previously considered distinctly unusual.

As the demographic and radiographic patterns of tuberculous pleurisy have evolved, so have the characteristics of the pleural fluid. Recent series have demonstrated pleural fluid neutrophilia to be more common then previously appreciated. In the 1973 landmark article by Light et al4 on the utility of cell counts in the differential diagnosis of pleural effusions, none of the 14 patients with TB had more than 50% PMNs. In contrast, 3 of 26 patients described in the 1991 series of Siebert et al5 had more than 95% PMNs and 15% of the patients of Epstein et al6 had more than 90% PMNs. Based on animal models and limited human data, neutrophilia of the pleural fluid has been attributed to acute infection, with expected rapid evolution to lymphocytosis. In rabbits, the neutrophilic phase of tuberculous pleural effusion lasts only 24 h,6 in humans, a 2-week time course has been described.7 Pleural fluid sampling earlier in the course of infection is unlikely to explain the increased prevalence of neutrophilic effusions in more recent series and clearly cannot explain our patient’s unilateral pleural fluid neutrophilia, which was stable over a 3-week period. Host factors other than acuity of infection must be invoked, and the coincident presence of a typical lymphocytic tuberculous effusion in this case localizes these factors to the pleural space. It is possible that the left pleural involvement occurred first, with resultant sequestration of all of the patient’s tuberculin-responsive T cells in this pleural space.8 Such a mechanism has been invoked to explain the initially negative PPD skin tests seen in up to one third of patients with tuberculous pleurisy. If sequestration of all reactive lymphocytes in the left effusion was the reason for the relative absence of lymphocytes in the right pleural space, though, we would expect a negative PPD; the patient’s positive skin test attests to the presence of circulating tuberculin-sensitive lymphocytes that could potentially have been recruited into the right pleural space. It is also possible that the atypical features of the right effusion resulted from coincident bacterial infection in that pleural space. Negative bacterial cultures, the failure of the patient to respond favorably to antibacterial therapy, the lack of change in the characteristics of the effusion despite two courses of antibiotics, and the need to invoke a second diagnosis all speak against this.

CONCLUSION

Pleural TB is a changing disease, both in terms of its demographics and, likely as a consequence, its features. Pleural effusion is occurring in an older population, in the setting of reactivation disease, and with cellular and biochemical features once thought atypical. The factors that determine the manifestations of disease in a given case remain poorly understood. This case, which we believe to be the first reported case of bilateral tuberculous pleural effusions of strikingly and persistently different cellular and biochemical characteristics, illustrates the newly recognized breadth of manifestations of tuberculous pleural disease and implicates local pleural space factors as one of their determinants.

REFERENCES


Central Alveolar Hypoventilation Syndrome (Ondine’s Curse) With Gastroesophageal Reflux*

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Congenital central hypoventilation syndrome (Ondine’s curse) is a rare disorder with lack of automatic control of ventilation during sleep. We have reported a case of Ondine’s curse in a patient who underwent

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