Case 8

The patient was a 55-year-old male with a 2-month history of fevers, night sweats, increased cough with sputum production, and a 25-lb (ca. 11-kg) weight loss. The patient denied intravenous drug use or homosexual activity. He had had multiple sexual encounters, "sipped" a pint of gin a day, was jailed 2 years ago in New York City, and had a history of gunshot and stab wounds. His physical examination was significant for bilateral anterior cervical and axillary adenopathy and a temperature of 39.4°C. His chest radiograph showed paratracheal adenopathy and bilateral interstitial infiltrates. His laboratory findings were significant for a positive HIV serology and a low absolute $CD4^+$ lymphocyte count.

The result of an acid-fast stain of sputum is seen in Fig. 1. Figure 2 shows the organism causing his infection after 6 weeks of incubation. The same organism was detected in bronchoalveolar lavage fluid from the right middle lobe.

1. What is bronchoalveolar lavage fluid? How is it obtained? What is its value as a diagnostic specimen?

2. Which organisms can be positive on an acid-fast stain?

3. Given his medical history, which organism is likely to be causing his infection? How does the finding that the patient is HIV positive affect this conclusion?

4. Which factors in his medical history do you think are important in his contracting this infection with an acid-fast bacterium?

5. What is a PPD test? What is its value in this patient? What additional tests would you order with a PPD test?

6. What infection control measures must be taken during this patient's hospitalization? What other issues are important in the management of this patient?

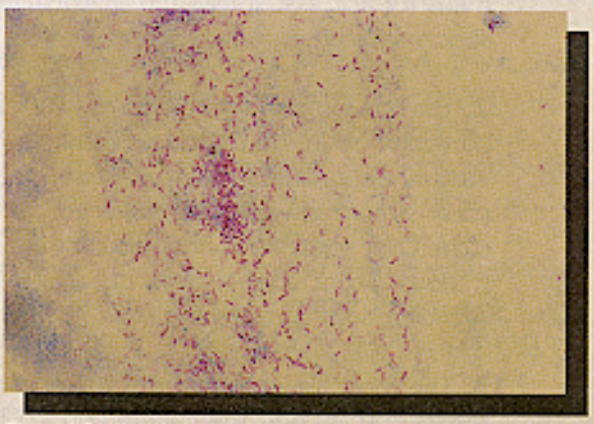

Figure 1

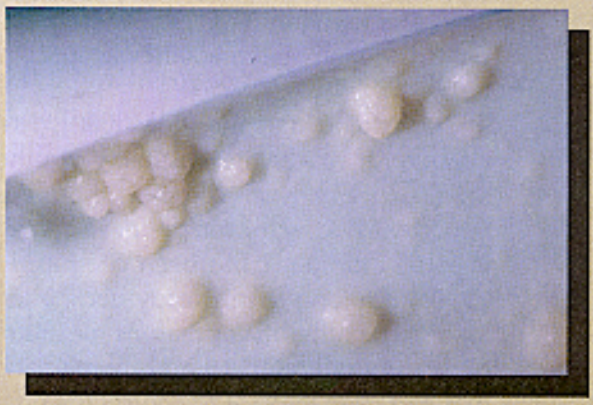

Figure 2

8 Case Discussion

1. Bronchoalveolar lavage is performed during bronchoscopy. The bronchoscope is wedged into the bronchus of the lobe in which disease is seen by radiographic examination or by visual inspection of the airway. Approximately 100 to 200 ml of nonbacteriostatic saline is injected through a channel in the bronchoscope into a specific lobe. This large volume of saline lavages the alveoli. The lavage fluid, containing inflammatory cells and, in cases of infection, infectious agents, is aspirated from the lung through the bronchoscope. This method is particularly useful in recovering viral agents and in detecting *Pneumocystis carinii*. This is a very effective way of collecting contents of the alveoli of the lung without these contents being contaminated with organisms from the upper airways (as would be seen with sputum). In patients without cough or with nonproductive cough, bronchoscopy is the simplest way to sample the lungs adequately. Of note, in obtaining respiratory specimens for acid-fast smear and mycobacterial culture, a post-bronchoscopy sputum specimen is often rewarding.

2. The most important organisms which are acid fast are mycobacteria (Fig. 1). The particular stain used was a Ziehl-Neelsen stain. A fluorescent acid-fast stain, auramine-rhodamine stain, is used in many laboratories in the United States. This stain is more sensitive and easier to perform and interpret than the Ziehl-Neelsen stain. Other organisms of clinical importance which are either completely or partially acid fast include *Rhodococcus equi*, *Nocardia* spp., and the protozoans *Cryptosporidium* spp. and *Isospora* spp.

3. The most likely organism is *Mycobacterium tuberculosis*. Both the acid-fast stain results (Fig. 1) and the culture (Fig. 2) are consistent with this organism. Further identification using a DNA hybridization technique confirmed its identity. *M. tuberculosis* grows quite slowly and may require as long as 6 to 8 weeks to grow on solid agar. The medium (Fig. 2) on which the isolate is growing is a Lowenstein-Jensen slant. This high-lipid medium was specifically designed for the isolation of mycobacteria.

The finding that the individual is HIV positive should not alter this diagnosis, although it makes the possibility of other mycobacteria, such as members of the *Mycobacterium avium* complex, more likely. Infection with HIV is recognized as an important risk factor for the development of tuberculosis (TB). In fact, TB in HIV-infected individuals has been cited as a major reason for the reversal in the early 1990s of a long-term, steady decline in the number of cases of TB in the United States. The other major reasons for this reversal include the increase in the number of cases of imported TB and the partial dismantling of the public health measures that had been in place to control the disease. This rising trend of TB infection is particularly striking in HIV-infected intravenous drug users.

One issue that has become a particular public health concern is the increasing numbers of *M. tuberculosis* isolates recovered from AIDS patients that are resistant to the first-line antituberculous drugs isoniazid and rifampin. Spread of multi-drug-

resistant organisms from this patient population to their caregivers has been reported. Also frequently seen in HIV-positive individuals are organisms of the *M. avium* complex, which often disseminate widely via the hematogenous route, with hepatic and bone marrow involvement.

4. Factors which put this patient at increased risk for TB are his HIV seropositivity, his alcoholism, and the fact that he had recently been jailed. This disease is more prevalent in individuals with any one of these risk factors. The presence of all three risk factors only increases the likelihood of his having active TB. His clinical presentation is also typical for TB except that apical regions of the lung are the most commonly affected in active disease. Cavitary lesions, which are frequently seen in normal hosts, are unusual in HIV-infected patients. This may reflect their immunocompromised state and inability to develop cell-mediated immune responses to the mycobacterial infection. HIV-infected patients are also at high risk for extrapulmonary TB.

5. A PPD test is a skin test used to screen individuals for *M. tuberculosis* infection. PPD is an *M. tuberculosis* antigen (purified protein derivative tuberculin) that is injected intracutaneously in the forearm with a tuberculin syringe. The forearm is examined at the site of injection 48 and 72 h later. In HIV-seronegative individuals who have no known close contact with TB-infected patients and have no other medical conditions or epidemiologic risk factors that increase the risk of TB infection, an area of induration of 15 mm or more is classified as a positive PPD test; these individuals should receive preventive therapy if their skin test has recently converted or if they are under 35 years of age. It should be noted that most PPD-positive patients are asymptomatically infected.

The immunosuppression which occurs as a result of HIV infection may lead to false-negative skin tests. When performing a PPD test on an HIV-positive patient, a concurrent control skin test for anergy (usually using a candidal or tetanus toxoid antigen) should be done to determine whether the patient is even capable of reacting to common antigens. Negative PPD tests are uninterpretable in anergic individuals. An area of induration of at least 5 mm in HIV-seropositive individuals, persons who have had recent close contact with individuals with active TB, or persons with fibrotic changes on chest radiographs consistent with healed TB meets the criteria for a positive skin test, but more definitive evidence of active disease should be sought as well. For those persons without HIV infection but with clinical or epidemiologic risk factors that would place them at increased risk for TB, induration of at least 10 mm is classified as a positive PPD. The epidemiologic risk factors that would place an individual at increased risk include being born outside the United States in an area with a high prevalence of TB, being a migrant farm worker or homeless person, being a resident of a prison, nursing home, or homeless shelter, or working closely with such individuals. Medical conditions that would make an individual more likely to progress from latent TB to active disease include malignancy, diabetes mellitus, and conditions for which the individual is receiving prolonged high-dose corticosteroid therapy.

6. *M. tuberculosis* is spread by respiratory droplets from infected individuals. Infection control measures to prevent the spread of this organism are based on this knowledge. Important components of respiratory isolation include housing patients supected or known to be infected with TB in a "negative-pressure" room with the door closed, and the use of respirators by individuals entering the infected patient's room. A negative-pressure room is one in which the flow of air is into instead of out of the room. Patients must remain in the room until it is proven that they are either not infected or no longer infectious. To prove a patient is no longer infectious, the patient must have negative acid-fast smears from three different sputum specimens obtained on different days. If the patient must leave the room, he or she must wear a surgical mask.

Besides infection control considerations, the other major factor in optimizing medical management is patient compliance with taking his/her antituberculous therapy. Effective antituberculous therapy requires months to complete. Because of its length, patients are rarely hospitalized for its duration. That means most antituberculous therapy is done in the outpatient setting, typically after the patient is no longer infectious. When patients are infected with *M. tuberculosis* which is resistant to multiple antimicrobial agents, the treatment regimen is not only extended but also complex. As a result, an important factor in antituberculous therapy is directly observed therapy (DOT). In DOT, a reliable individual, anyone from a health care worker to a prison guard to a worker in a homeless shelter, watches the infected individual take his or her medicine to ensure adherence to the appropriate treatment regimen. Public health officials have the option of incarcerating infected individuals who refuse to follow their treatment regimen, to ensure compliance.

There are other important issues concerning prevention of *M. tuberculosis* transmission. The interested reader should refer to the Centers for Disease Control and Prevention document "Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-Care Facilities," published Oct. 28, 1994, in *Morbidity and Mortality Weekly Report.*

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