Prolonged Survival of an HIV-Infected Patient with Multidrug-Resistant
Mycobacterium bovis Infection Treated with Surgical Resection

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We describe a case of multidrug-resistant tuberculosis due to Mycobacterium bovis in a human immunodeficiency virus–infected woman with good immunologic status. The patient presented with a hard mass measuring 10 cm in diameter on the lower left ribs and a lung nodule measuring 3 cm in diameter in the left superior lobe. No adequate pharmacological treatment was available. Both lesions were surgically resected. The patient has remained asymptomatic (without fever, cough, lymphadenopathy, or cutaneous masses) for 20 months, after discharge from the hospital.

The enhanced incidence and susceptibility to tuberculosis in HIV-infected patients has dramatically changed the epidemiology of tuberculosis and has increased the risk of nosocomial transmission in health care facilities [1, 2]. Although Mycobacterium bovis is the main organism responsible for tuberculosis in cattle, during the last decade its involvement as a causative agent of tuberculosis in HIV-infected patients has been observed in several countries [3].

Three related nosocomial outbreaks of multidrug-resistant tuberculosis (MDR-TB) caused by M. bovis in patients infected with HIV have been reported in Spain [4–6]. In 2 hospitals, the same strain was responsible, and, in the case of the third outbreak, it was supposed that the same strain was involved, but this was not definitively confirmed. The strain responsible was resistant to nearly all the drugs tested [7, 8]. All HIV-infected patients died, despite treatment with multiple first- and second-line antituberculosis drugs. It has been suggested that these outbreaks were controlled because control policies were implemented in these hospitals and because the time between acquisition of the infection and death was brief for the majority of patients [8].

A late wave of cases among immunocompetent persons exposed and infected during outbreaks of MDR-TB could be expected in the future [9]. It may be very difficult to administer efficacious treatment to these patients. We describe a singular case of an HIV-infected patient with MDR-TB due to M. bovis who had prolonged survival.

Case report. A 35-year-old woman was admitted to our hospital (Hospital Universitario Puerta de Hierro, Madrid) in December 2000 because of a 3-month history of productive cough, yellowish sputum, and low fever. The patient had been infected with HIV since 1994 and, since 1996, had been receiving treatment with zidovudine, lamivudine, and didanosine at another hospital in the same town, with good immunologic and virologic responses. Her CD4 cell count was 942 × 10^6 cells/L, and her HIV load in plasma was fully suppressed (<50 copies/mL). Chest radiography showed a cavitory infiltrate (2 cm in diameter) in the left upper lobe. Direct microscopy of sputum collected at the time of hospital admission was positive for acid-fast bacilli. Therapy with isoniazid (300 mg/day), rifampicin (600 mg/day), pyrazinamide (1500 mg/day), and ethambutol (900 mg/day) was given for 2 months without any clinical improvement. A sputum culture was positive for M. bovis resistant to isoniazid, rifampin, pyrazinamide, ethambutol, streptomycin, para-aminosalicylic acid, clarithromycin, clysolserine, ethionamide, ofloxacin, capreomycin, and amikacin. Six weeks later, Löwenstein culture of a sputum specimen was negative for mycobacteria. The patient was lost to clinical follow-up after discharge from our hospital.

In February 2002, the patient was again admitted to our hospital because of a mass on her left thoracic wall that demonstrated slow progressive growth. At admission, her temperature was 37.4°C, her pulse rate was 88 beats per minute, and her respiratory frequency was 24 breaths per minute. On physical examination, the patient was alert, fully oriented, and able to converse. A painless hard mass (10 cm in diameter) was palpated on the left lower ribs under the left breast. Findings of lung, heart, abdomen, arm, and leg examinations were all normal. The hematocrit was 31%, the mean corpuscular volume was 86 μm³, the WBC count was 5300 cells/mm³ (68% neutrophils, 26% lymphocytes, and 6% monocytes), and the platelet count was 291,000 cells/mm³. Results of plasmatic biochemical analysis were normal. A chest radiograph showed a
spiculated and noncalcified nodule measuring 3 cm in diameter in the left superior lobe. A CT scan and MRI of the chest confirmed that the nodule was without lymphadenopathy (figure 1) but revealed an image measuring 9 cm in diameter suggestive of a purulent collection in the thoracic wall (figure 2). Sputum and exudative specimens were obtained by lung nodule and thoracic mass puncture; Ziehl-Nielsen staining of the specimens revealed *M. bovis*, and a Löwenstein culture yielded the same *M. bovis* strain isolated at baseline. DNA typing analysis indicated that this *M. bovis* strain was the same as that which caused 2 previously reported outbreaks in 2 Spanish hospitals in the 1990s, which had the same pattern of drug resistance [4, 5]. This strain had two IS6110 bands at the same positions and identical spoligotyping patterns. The patient underwent surgical resection of the lung nodule (posterior segmentectomy) and the thoracic mass, and then the thoracic wall was reinforced using a muscle flap. Chemotherapy was not administered because no adequate treatment was available. During the period of hospitalization, the patient was placed in a negative air-pressure room to avoid nosocomial spread.

During the 20 months after discharge from the hospital, the patient remained asymptomatic, with no clinical or radiological signs of relapse and with a good immunologic and virologic response to antiretroviral treatment. Her husband, who was HIV-seropositive, had died after admission to a hospital in 1994, during an MDR-TB outbreak [6].

**Discussion.** There are some remarkable features in this case report. First, the results of spoligotyping and restriction fragment–length polymorphism patterning suggest that the patient became infected with the same *M. bovis* strain responsible for nosocomial outbreaks in some Spanish hospitals between 1991 and 1998 [4–6]. The patient developed MDR-TB 6 years after her husband had been admitted to a hospital during an MDR-TB outbreak. He died in 1994. Our patient may have acquired her infection at that hospital or at home while she was caring for her husband. The present case highlights the risk to people who have contact with patients with MDR-TB and the rationale for improving community epidemiologic policies in order to diminish the number of new MDR-TB cases in the population. Knowledge of past contact with a patient admitted to a hospital that was affected by an MDR-TB outbreak is of prime importance. It has been demonstrated that exposure to an infected patient in a hospital without an isolation policy for patients with respiratory disease, as well as a CD4 cell count of <500/µL, is associated with an increased risk of developing MDR-TB due to *M. bovis* in HIV-infected patients [1].

Second, there was a prolonged delay between the appearance of the cavitary infiltrate and the time at which the patient was admitted to our hospital with a thoracic mass. The patient’s good immunologic status could have delayed the progressive development of clinical signs of MDR-TB. Nevertheless, some infected, immunocompetent patients had a similar prolonged clinical course, also with early clinical improvements, despite apparently inappropriate treatment [2, 10]. This is very different from the rapid development of MDR-TB and the high mortality that characterized most cases in HIV-infected patients (with a poor immunologic status) after hospital contact with an infectious patient [2, 4]. In fact, to our knowledge, the present case is the only instance of an HIV-infected patient with MDR-TB due to this strain of *M. bovis* who remained alive >1 year after diagnosis.

It is also noteworthy that the patient had an extrapulmonary illness, but only 2 body sites that were affected could be completely surgically resected. On the basis of our experience, surgical treatment should be considered for patients with similar cases, provided the lesions are completely resectable and that
There was considerable delay in the definitive treatment of this patient because she did not follow medical advice and, for several months, was lost to clinical follow-up. However, the patient finally received treatment that controlled the clinically active sites of infection. In addition, this patient has an increased risk of MDR-TB reactivation in the future, in the event of immunologic failure due to an advanced stage of her HIV infection or for other reasons, such as advanced age, use of corticosteroids, or receipt of antineoplastic chemotherapy.

This encouraging result in an HIV-infected patient with MDR-TB supports the use of surgical treatment in similar cases in patients who cannot receive appropriate chemotherapy at a sufficiently early stage of the disease, before extensive dissemination of tuberculosis occurs.

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References