Transmission of Multidrug-Resistant *Mycobacterium bovis* to an Immunocompetent Patient

Human tuberculous infections caused by *Mycobacterium bovis* are relatively rare. Most cases among HIV-infected patients have been reported in England, France, and the United States [1], with human-to-human transmission [2]. Infections due to multidrug-resistant *M. bovis* are extremely rare, but recently two nosocomial outbreaks involving HIV-infected patients have been described at two different hospitals in Spain [3, 4]; in one hospital, there was transmission to a foreign, HIV-positive patient who stayed in Spain briefly [5]. However, such transmission to immunocompetent patients is extremely rare. We describe herein transmission of multidrug-resistant *M. bovis* to an immunocompetent patient.

A 46-year-old, heterosexual, HIV-negative, Spanish man was referred to our hospital in March 1996. He had a 2-month history of pleuritic chest pain and fever (temperature, 38°–39°C) accompanied by a 7-kg weight loss. He denied exposure to mycobacterial disease. A chest radiograph showed a shadow in the right upper lobe with air bronchogram and a few cavitations inside. A CT scan of the thorax disclosed a shadow in the right lower lobe, a right pleural effusion, and pretracheal lymphadenopathy. A diagnosis of pulmonary tuberculosis was made on the basis of a positive auramine-fluorochrome stained smear of a bronchial brushing specimen. Treatment with isoniazid (300 mg/d), rifampin (600 mg/d), ethambutol (1,200 mg/d), and pyrazinamide (1,500 mg/d) was initiated. The latter two agents were discontinued after 2 months, and treatment with isoniazid and rifampin was maintained for 4 additional months, after which time he was asymptomatic. Because no sputum was produced during the treatment, no microbiological controls were done.

After 5 weeks of therapy, a culture positive for *Mycobacterium tuberculosis* complex (3 cfu) was obtained in Löwenstein-Jensen medium without sodium pyruvate and with 2-thiophenecarboxylic acid hydrazide, although these two media are usually inhibitory for *M. bovis* but not for *M. tuberculosis*. The strain was identified by using DNA-RNA hybridization (AccuProbe; Gen-Probe, San Diego, CA). At the end of treatment (September 1996), a chest radiograph showed progression of abnormalities and several small nodules in the left upper lobe. In November 1996, repeated bronchoscopy was performed. At this time, pulmonary biopsy, bronchial washing, and bronchial brushing samples were obtained; staining of these specimens was negative. In December 1996, the patient became symptomatic; a few sputa produced at that time stained positive for mycobacteria. A new treatment regimen with isoniazid (300 mg/d), streptomycin (750 mg/d), ethambutol (1,200 mg/d), rifampin (600 mg/d), ofloxacin (400 mg b.i.d.), and pyrazinamide (1,500 mg/d) was instituted; the latter was discontinued after 10 weeks.

Treatment was maintained until susceptibility test results were available, including those for the baseline strain and the last-cultured strain. Cultures of all the bronchoscopy samples and sputa yielded *M. tuberculosis* complex in 4 weeks, and all strains were resistant to isoniazid, rifampin, streptomycin, ethambutol, and pyrazinamide. Because multidrug-resistant *M. bovis* was suspected, the strain was sent to two reference centers for molecular typing and in vitro susceptibility tests for second-choice drugs. The *M. bovis* strain was also resistant “in vitro” to kanamycin, ethionamide, rifabutin, ofloxacin, amikacin, and clarithromycin.

The multidrug-resistant strain was typed by use of spoligotyping and restriction fragment length polymorphism (RFLP) analysis.

![Computer images of spoligotyping of *Mycobacterium tuberculosis* complex strains: *M. tuberculosis* H37rv, *M. bovis* BCG, *M. bovis* 1 responsible for the outbreak described in [4], and *M. bovis* 2 isolated from the immunocompetent patient in the present study.](image-url)

## References


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Microgranulomatous Aspergillosis in a Patient with Chronic Granulomatous Disease: Cure with Voriconazole

To our knowledge, invasive aspergillosis with a micronodular presentation has been described only for patients with chronic granulomatous disease (CGD). We report a case in which cure was achieved after treatment with voriconazole.

A 30-year-old man with X-linked CGD was admitted to the hospital because of fever and cough. Before prophylaxis with co-trimoxazole and IFN-γ was instituted, he had had many infections. Recurrent bladder granulomas led to impaired renal function. One week before admission, he developed a fever (temperature, 39.5°C) preceded by chills. On physical examination 4 days later, he appeared only slightly ill; his temperature was 38.9°C and a few slightly enlarged submandibular glands were noted. Laboratory evaluation revealed an elevated erythrocyte sedimentation rate (98 mm/h), leukocytosis (leukocyte count, 13 × 10⁹/L), and leukocyturia. A chest radiograph showed only old fibrotic changes in the right middle field. Ciprofloxacin, 750 mg b.i.d., was prescribed.

Three days later the patient was admitted because of persisting fever and a productive cough without dyspnea. Cultures of blood, sputum, and urine performed earlier were negative. A repeated chest radiograph was obtained, and review of both radiographs showed a micronodular pattern. Blood gas analysis revealed normoxia and slight hypcapnia. Lung function testing showed restriction and a diminished CO transfer factor. Indium ¹¹¹ (¹¹¹In)–IgG scintigraphy showed diffusely enhanced uptake in both lungs. Cultures of the bronchoalveolar lavage (BAL) fluid yielded several colonies of *Aspergillus fumigatus*. A video-assisted thorascopic lung biopsy was performed. Because of the impaired renal function, therapy was started with voriconazole, 200 mg b.i.d. orally. Prophylaxis with co-trimoxazole and IFN-γ was continued.

The lung biopsies were characterized histopathologically by the presence of randomly scattered, nonconfluent, noncaseating granulomas (< 0.1 mm). Centrally located septate hyphae were seen in some granulomas. Angioinvasion by fungi was not observed. Cultures of the lung biopsy specimen yielded *A. fumigatus* and remained negative for mycobacteria. Serology for anti-