Pneumonia and Bacteremia Due to *Mycobacterium celatum* Masquerading as *Mycobacterium xenopi* in Patients with AIDS: An Underdiagnosed Problem?

Christine A. Zurawski, Gary D. Cage, David Rimland, and Henry M. Blumberg

A newly described species of mycobacteria, *Mycobacterium celatum*, has rarely been reported as a cause of localized and disseminated human disease and can easily be misidentified as *Mycobacterium xenopi* when identification is based on biochemical testing alone. We report two cases of pneumonia and bacteremia due to *M. celatum* in patients with AIDS. In one case, diagnosis and initiation of therapy were delayed by misidentification of the infecting organism as *M. xenopi*. Genomic analysis or high-performance liquid chromatography is necessary to distinguish the two species. The finding in our two cases and a review of existing literature indicate that pulmonary disease may be an important manifestation of infection with *M. celatum*, especially in patients with AIDS. Further studies are needed to determine the incidence and clinical relevance of this organism in patients with AIDS and the optimal treatment regimens.

Nontuberculous mycobacterial infections, especially those due to *Mycobacterium avium* complex (MAC), are common in patients with AIDS [1]. A newly described species of mycobacteria, *Mycobacterium celatum*, has rarely been reported as a cause of localized and disseminated disease in patients with AIDS. *M. celatum* can easily be misidentified as *Mycobacterium xenopi* on the basis of conventional biochemical testing [1]. Genomic analysis or HPLC is necessary to distinguish the two species. We describe two patients with AIDS who had pneumonia and bacteremia due to *M. celatum*, which in one case was initially identified as *M. xenopi*.

Case Reports

**Patient 1.** A 40-year-old man was admitted to our hospital for evaluation of pneumonia with complaints of weakness, fever, increased sputum production, and worsening shortness of breath. He had a 2-year history of AIDS and a CD4+ lymphocyte count of 1/mm³ at the time of admission. He was receiving fosfamet for retinitis due to cytomegalovirus, fluconazole for esophageal candidiasis, and trimethoprim-sulfamethoxazole as prophylaxis against *Pneumocystis carinii* pneumonia.

Four months before admission, the patient had chest roentgenography performed, which revealed a left-lower-lobe infiltrate. He was treated at that time with a third-generation cephalosporin. Routine sputum cultures were negative. Smears of sputum were negative for acid-fast bacilli (AFB), but AFB cultures subsequently yielded an organism that was identified as *M. xenopi* (by standard biochemical testing done at the local reference laboratory). Three months before admission, sputum cultures for AFB again yielded an organism identified as *M. xenopi*.

One month before admission, he presented because of shortness of breath, and worsening of his left-lower-lobe infiltrate was evident on a chest roentgenogram. He underwent bronchoscopy, and stains for AFB were positive. He left the hospital against medical advice before any treatment was begun. Cultures of bronchoalveolar lavage fluid yielded an organism identified as *M. xenopi*.

On admission to the hospital, the patient was cachectic and appeared acutely ill. His temperature was 38.8°C, and rales were noted at the lung bases bilaterally. Chest roentgenography showed persistence of a left-lower-lobe infiltrate and the intervallic appearance of a right-lower-lobe infiltrate (figure 1). Laboratory tests revealed the following values: WBCs, 1,000/mm³, with 2% band forms, 26% polymorphonuclear cells, 38% monocytes, and 34% lymphocytes; hemoglobin, 6.4 g/dL; sodium, 126 mEq/L; urea nitrogen, 12 mg/dL; creatinine, 0.5 mg/dL; lactate dehydrogenase, 199 U/L; total protein, 5.4 g/dL; and albumin, 1.8 g/dL. Acid-fast stains of the sputum were again positive.

Because of the protracted nature of the patient’s symptoms and the repeated isolation of *M. xenopi* from the sputum, therapy was begun with isoniazid, rifampin, ciprofloxacin, and clarithromycin. A blood culture for AFB was also positive, and the pathogen was subsequently identified by the local reference laboratory as *M. xenopi*. An isolate was referred to the Arizona State Laboratory (Phoenix) for HPLC analysis and was identified as *M. celatum*. Susceptibility testing revealed resistance to isoniazid, rifampin, streptomycin, ethambutol, and ciprofloxacin. Susceptibility testing for clarithromycin was not performed. The patient was lost to follow-up after discharge; therefore, response to therapy could not be evaluated.
M celatum vs. M xenopi Infection in Patients with AIDS

Figure 1. A radiograph of the chest of patient 1, a man with AIDS whose recent cultures had yielded an organism identified as M. xenopi, shows bilateral basilar pulmonary infiltrates.

Patient 2. A 32-year-old man with AIDS and a CD4+ lymphocyte count of 10/mm³ was admitted because of a right-upper-lobe cavitary lesion and fever. Routine sputum cultures and AFB smears were negative. The patient was treated with cefuroxime and became afebrile. Sputum and blood cultures for AFB subsequently yielded M. celatum. These cultures were submitted to the West Haven Veterans Administration Reference Laboratory (West Haven, CT), which uses HPLC as a means of species identification.

Before initiation of therapy 2 months later, another blood culture for AFB yielded M. celatum and MAC. The patient was treated with clarithromycin and ethambutol. Susceptibility testing revealed the M. celatum isolate to be resistant to isoniazid, rifampin, streptomycin, ethambutol, and clofazimine. This isolate was susceptible to clarithromycin and ciprofloxacin. After initiation of therapy, no further blood or sputum cultures yielded M. celatum. The patient died 4 months later, but it is unclear how M. celatum infection contributed to his death.

Discussion

M. celatum (the species name means “hidden”) is a slowly growing, nonphotochromogenic Mycobacterium species whose biochemical characteristics and colony morphology resemble those of MAC and M. xenopi. M. celatum produces small, nonpigmented, opaque colonies and may produce microcolonies similar to those of M. xenopi [2, 3]. Isolates from the two cases presented herein fit these criteria as well as previously reported biochemical characteristics, including positive arylsulfatase and pyrazinamidase tests and negative nitrate reduction, niacin, and catalase tests. Butler et al. reported growth at 3 weeks, but only at 37°C [3]. Tortoli et al. reported growth at
45°C [2], while our isolates exhibited growth at both 35°C and 42°C. However, cultures held for 5 weeks in the series of Butler et al. [3] grew to varying degrees at all temperatures tested (27°, 30°, 33°, 37°, 42°, and 45°C).

*M. celatum* has also been reported to “masquerade” as *Mycobacterium tuberculosis* by cross-reacting with commercially available genetic probes used for rapid identification of mycobacteria. Butler et al. examined 20 strains of *M. celatum* and found that 40% reacted with the acridinium ester–labeled AccuProbe (Gen-Probe, San Diego) [4]. However, none of the strains evaluated by Butler et al. in the original description of the species cross-reacted with the genetic probes for *M. tuberculosis* or MAC, neither with use of radioactive and nonradioactive Gen-Probe products nor with Snap X probes (Syngene, San Diego) [3].

Tortoli et al. reported no cross-reactivity of two *M. celatum* isolates with Gen-Probe probes for *M. tuberculosis* or MAC [2]. Neither isolate from the two cases presented here reacted with genetic probes (AccuProbe) for *M. tuberculosis* or MAC. Although the striking difference in the susceptibility patterns of *M. celatum* and *M. tuberculosis* should alert the clinician to a possible error in species identification, the potential for misdiagnosis needs further clarification.

Sequencing of 16s RNA and HPLC have shown that *M. celatum* is a distinct species and differs from *M. xenopi* and MAC in its mycolic acid composition [2]. *M. celatum* can be misidentified as *M. xenopi* when routine biochemical testing alone is used as a means of identification, as occurred in our first case. HPLC is the most reliable way to distinguish *M. celatum* from *M. xenopi* [3]. Figure 2 shows the HPLC pattern of the *M. celatum* isolate from patient and the HPLC pattern of an *M. xenopi* isolate recovered from an unrelated patient. The susceptibility pattern of *M. celatum* also differs from that of *M. xenopi*. While *M. xenopi* is usually susceptible to isoniazid and rifampin, *M. celatum* is uniformly resistant to most anti-tuberculous drugs [3]. All 24 isolates of *M. celatum* tested by Butler et al. [3] were resistant to isoniazid, rifampin, and pyrazinamide, and 33% were resistant to ethambutol. All of the isolates were susceptible to ciprofloxacin. It is interesting that the *M. celatum* isolate from case 1 was resistant to ciprofloxacin.

*M. celatum* has recently been reported as an opportunistic pathogen in a few patients with AIDS [2, 5]. Our cases, in which *M. celatum* was isolated repeatedly from sputum, bronchial washings, and blood, are the second and third reported cases of pulmonary infection due to *M. celatum* and the first two to result in bacteremia. Tortoli et al. described a patient with AIDS who had a CD4+ cell count of 33/mm³, hepatomegaly, and a left-upper-lobe cavitary lesion [2]. *M. celatum* was isolated from the patient’s sputum. Another patient with AIDS, whose CD4+ cell count was 27/mm³, was also described; this patient experienced several episodes of *M. celatum* bacteremia [1, 5].

![Figure 2](image-url)

**Figure 2.** HPLC patterns demonstrating mycolic acid content of *M. xenopi* (A) and *M. celatum* (B). HPLC pattern B is from case 1. HMW = high molecular weight standard.

To our knowledge, these three cases are the only reported ones of *M. celatum* bacteremia. All cases of bacteremia involved patients with AIDS whose CD4+ lymphocyte counts were very low (<50/mm³). Butler et al. has described 24 isolates of *M. celatum* recovered from reportedly ill patients, but information about clinical presentations was not available [3]. Sixteen of the 24 isolates (66%) were from sputum or bronchial washings, and 8 of the 24 isolates (33%) were from patients with HIV infection. The HIV status of some of the patients reported by Butler et al. was not known. Other sources of isolates from this series were blood, vertebral bone, and stool.

*M. celatum* has also been reported to cause lymphadenitis in an immunocompetent child [6]. The reports by Butler et al. and our experience suggest that pulmonary disease may be an
important manifestation of infection with *M. celatum*, especially in patients with AIDS.

Our first case illustrates that *M. celatum* can easily be misdiagnosed as *M. xenopi*. When HPLC is used routinely to identify mycobacteria, as in the second case, misidentification on the basis of biochemical testing does not occur. In light of these findings, if serious clinical disease due to *M. xenopi* is suspected, confirmation of the species by HPLC should be considered and antibiotic susceptibility testing should be performed with an extended panel of drugs. The need to distinguish between *M. celatum* and *M. xenopi* does have potential therapeutic implications, given the different susceptibility patterns of *M. celatum* and *M. xenopi*. *M. celatum* is more resistant to antituberculous drugs.

Isolation of *M. xenopi* from the sputum, blood, bone marrow, and stool of patients with AIDS has been reported [7]. How many, if any, of these infections were actually due to *M. celatum* is unknown, but, given our experience, we suspect some of these cases may have been due to *M. celatum*, which was misdiagnosed as *M. xenopi*.

Epidemiologic studies regarding the reservoir and clinical presentations of *M. celatum* have not been published. Further studies are needed to determine the incidence and clinical relevance of this organism in patients with AIDS and optimal treatment regimens.

References