Remission of Cutaneous Mycobacterium haemophilum Infection as a Result of Antiretroviral Therapy in a Human Immunodeficiency Virus–Infected Patient


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We describe the first Mycobacterium haemophilum infection that occurred in a patient with human immunodeficiency virus in Germany and report 7 newly diagnosed cases of M. haemophilum infection. In the former case, a local M. haemophilum skin infection resolved as a result of successful antiretroviral therapy only; however, that clinical outcome may not be possible for more invasive forms of the disease.

Cutaneous infections with potentially pathogenic mycobacterial species are of importance for the differential diagnosis of skin lesions in HIV-infected patients. Increasing numbers of Mycobacterium haemophilum infections are documented in immunocompromised subjects with an array of clinical conditions. M. haemophilum infections have been reported especially in patients with lymphoma or HIV, after incisions or surgical procedures, and in organ transplant recipients [1, 2]. M. haemophilum has been recovered from otherwise healthy children with cervical lymphadenopathy, as well as from immunocompetent elderly patients [3–5]. To our knowledge, data have been obtained for 113 cases of M. haemophilum infection since its first description in 1978 [6–8]. These infections occurred in various geographic areas, but few have been described in Europe [7, 8].

According to the National Reference Center for Mycobacteria (Borstel, Germany), 5 cases of M. haemophilum infection were reported in Germany in 1999, and 2 cases in 2000. All these cases occurred in patients who were immunocompromised for reasons other than HIV infection. Clinical manifestations of disease due to M. haemophilum infection consisted of skin lesions (in 4 patients), lymphonodular infection (in 1 patient), and infected bones (in 2 patients).

In this report, we describe what is, to our knowledge, the first case in Germany of M. haemophilum infection in an immunocompromised patient with HIV-1 infection. According to the literature, the treatment of M. haemophilum infections requires initiation of a potent antibiotic therapy regimen. Data from susceptibility testing of M. haemophilum isolates indicate that it is susceptible to amikacin, ciprofloxacin, clarithromycin, and rifampin [7, 8]. In addition, Moulsdale et al. [9] have suggested that sulfamethoxazole might be beneficial for treatment of M. haemophilum infection. However, relapses of infection after completion of different therapy regimens and drug resistance against ethambutol and isoniazid have been repeatedly reported [8]. Despite these reports, we observed in a patient with verified local M. haemophilum infection a complete remission without initiation of a specific antimycobacterial therapy regimen.

Case report. A 30-year-old black woman who was originally from Ghana and had an untreated HIV-1 infection first presented to the Institute for Interdisciplinary Infectiology and Immunology, Hamburg, Germany, in 2000. The patient had lived in France since 1991 and moved to Germany in 1998. During her 2-year stay in Germany, she had worked as a house cleaner. Her dermatologic history included no skin diseases or conditions. In June 2000, the patient tested positive for HIV-1 infection by use of ELISA and PCR. Initial immunological laboratory values, measured by routine flow cytometry, revealed a CD4+ lymphocyte count of 10 cells/µL (1% of total lymphocyte count). A virus load of 102,000 copies/mL was determined with use of the Roche Amplicor ultrasensitive quantitative PCR detection assay (Roche).

In July 2000, two indurated, ulcerating, and secreting skin nodules (each ∼2 cm in diameter) developed from circumscribed and exanthematic skin areas near the right elbow. At the end of June 2000, the subject had been admitted to the hospital because of weight loss, diarrhea, vomiting, fatigue, and weakness. She was observed in the infectious disease ward until her condition had improved, and she was discharged before visible skin nodules appeared, after 7 days. She had complained about generalized pruritus for 1 month before and during her
stay at the infectious disease ward, but no fever or pain in the area of the skin nodules occurred. Swabs of secretions from the nodules were obtained for bacterial culture, and tissue specimens from skin nodules were obtained and analyzed.

The initially assumed diagnosis, bacterial angiomatosis, was excluded by PCR. Microtome sections of tissue specimens were stained with hematoxylin and eosin and displayed granulomatous areas surrounded by a strong, nonspecific inflammation. However, numerous acid-fast bacilli became visible in macrophages with use of the Fite-Faraco staining method (figure 1). Swabs of both ulcerated nodules were obtained on different days for mycobacterial culture. However, bacilli failed to grow on Loewenstein-Jensen culture media, except in slanted test tubes containing iron-supplemented Loewenstein-Jensen medium that were incubated at 32°C. By means of direct PCR and 16S rDNA sequencing, _M. haemophilum_ was identified from the specimens that were also used for culture (figure 2) [10].

Antiretroviral therapy (ART) to treat HIV-1 infection was initiated at the end of July 2000; the patient received stavudine (40 mg orally b.i.d.), lamivudine (150 mg orally b.i.d), indinavir (800 mg orally b.i.d), ritonavir (100 mg orally b.i.d.), and primary prophylaxis against _Pneumocystis carinii_ pneumonia with trimethoprim-sulfamethoxazole (400 mg/80 mg orally q.d.). After 6 weeks of ART, the local _M. haemophilum_ infection began to resolve progressively; a complete remission was observed after 5 months of therapy. The patient’s CD4+ cell count was 123 cells/µL (8%) after 5 months of ART. No relapse of infection appeared at monthly follow-up visits during a period of 14 months.

**Discussion.** In the cases described in the literature, specific antimycobacterial therapy was administered to all _M. haemophilum_-infected individuals. In the case we describe here, complete resolution of _M. haemophilum_ infection was achieved after initiating an ART regimen with 2 nucleoside reverse-transcriptase inhibitors and boosted protease-inhibitor therapy, but without specific antimycobacterial treatment. Many different opinions about appropriate antimycobacterial therapy strategies are currently being discussed because of reports of relapses and resistance toward available antimycobacterial drugs [2, 8]. Effective regimens containing clarithromycin, amikacin, ciprofloxacin, or streptomycin have been reported, but so have instances of relapse after discontinuation of therapy [7, 8]. As an alternative, some authorities recommend curative skin surgery; however, this treatment is performed only in rare cases with few infected sites only [11].

For the case we describe here, a specific antimycobacterial therapy regimen was not given to the patient, because remission had already begun at the same time that diagnosis was verified by the results of mycobacterial cultures and PCR. The remission of cutaneous _M. haemophilum_ infection as a result of effective first-line ART therapy alone is unusual, and does not indicate that the infection will not reoccur later. Consequently, immunological laboratory values must be determined at regular follow-up visits for HIV-infected subjects. These laboratory val-

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**Figure 1.** Intracytoplasmically located _Mycobacterium haemophilum_ bacilli in macrophages. Note disseminated and single distributed bacilli (arrows). Microtome section from skin specimen with Fite-Faraco staining and imaged by light microscopy (original magnification, ×1000; a full-color version is available in the on-line edition of this article).
ues are the primary parameters used to estimate the risk of opportunistic infections, such as those due to mycobacteria. Sufficient recovery of the immune system and of cell-mediated immune capability in HIV-infected patients receiving ART is a long-term process and might take several months. Hence, we assume that a strong local inflammatory and reconstructive tissue reaction, supported by the beginning of immune-system reconstitution as a result of ART, is responsible for the successful outcome in the case we describe.

*M. haemophilum* infection may often be undiagnosed because routine microbiological techniques (i.e., mycobacterial culture on standard culture media, such as Loewenstein-Jensen media incubated at 37°C) are insufficient to detect it, because *M. haemophilum* grows only selectively on ferric ion–supplemented culture media and requires incubation at a temperature of 30°C–32°C. Thus, we recommend parallel diagnostic processing for tissue specimens obtained from infected patients. Tissue specimens should be obtained for performance of histopathologic testing and effective staining (i.e., Ziehl-Neelson or Fite-Faraco staining). Tissue specimens should also be tested for nontuberculous bacteria by means of culture and PCR [10].

Immunocompromised patients with specimens positive for acid-fast bacilli and negative for mycobacteria (e.g., *Mycobacterium tuberculosis* and *Mycobacterium avium-intracellulare*) should also be assessed for rare atypical mycobacterial species. Specimens should be tested by specialized laboratories that have experience in mycobacterial diagnostics and equipment suitable for performing PCR. Effective ART may reverse HIV-related immunosuppression, resulting in resolution of opportunistic mycobacterial infections. However, the improvement we noted was in cutaneous disease, and, therefore, the findings may not be applicable to more invasive forms of mycobacterial disease.

**References**