Resolution of Mycobacterium avium Complex Bacteremia Following Highly Active Antiretroviral Therapy

A 40-year-old HIV-positive man presented to the AIDS Reference Center in Santos, São Paulo, Brazil, in August 1996, complaining of a 1-month history of fever, night sweats, weight loss, and productive cough. On physical examination a severely edematous penis with several white plaques over the glans was noted. A fundoscopic examination showed white spots with fuzzy edges and hemorrhages bilaterally, indicative of cytomegalovirus (CMV) retinitis. Laboratory studies revealed the following values: hematocrit, 38%; WBC count, 4,500 cells/mm³; and platelet count, 168,000/mm³. The CD4 cell count was 23/mm³; CD3 cell count, 524/mm³; and CD8 cell count, 474/mm³. A chest radiograph showed a diffuse interstitial infiltrate, with intensification of the perihilar regions. The alkaline phosphatase level was 121 IU/L (normal level, 65–300 IU/L); aspartate aminotransferase, 23 IU/L (normal level, 14–41 IU/L); alanine aminotransferase, 17 IU/L (normal level, 5–35 IU/L); and lactate dehydrogenase, 644 IU/L (normal level, 150–360 IU/L). Routine blood cultures for bacteria and for mycobacteria were performed; 5 mL of blood were inoculated into a BACTEC 13A vial (Becton Dickinson, Sparks, MD) and 10 mL were inoculated into an Isolator tube (Wampole Laboratories, Cranbury, NJ) and processed per the manufacturer’s directions. Biopsy specimens of the penile lesion were obtained. Lung biopsies were obtained via bronchoscopy. Both tissues showed cytomegalic inclusion bodies indicative of CMV infection, and iv ganciclovir therapy was instituted on 12 August. Antiretroviral therapy (indinavir, 800 mg t.i.d., zidovudine, 200 mg t.i.d., and didanosine, 200 mg b.i.d.) was begun on 20 August.

The patient’s condition improved gradually and his fever and night sweats resolved by mid October. On 1 November, the CD4 cell count was 245/mm³; the CD3 cell count was 973/mm³; and the CD8 cell count was 640/mm³. On 2 February 1997, the CD4 cell count was 371/mm³; the CD3 cell count was 1,377/mm³; and the CD8 cell count was 896/mm³. Intravenous ganciclovir was continued once daily five times a week until 10 April 1997, when it was discontinued because the CD4 cell count was increased to >300/mm³.

The BACTEC 13A vial was read on a weekly basis by use of the BACTEC 460 system (Becton Dickinson) and showed a very slow increase in growth index (GI) readings, from <10 to 45 over a 15-week period, and then became positive (GI-648) at week 16. Ziehl-Neelsen staining at that time showed numerous acid-fast bacilli, and subcultures yielded Mycobacterium avium complex (MAC). The Isolator cultures yielded a single colony of MAC, and a sputum specimen collected in August 1996 also yielded MAC.

Because the patient’s CD4 cell count had increased significantly by the time his mycobacteremia was detected, antimycobacterial therapy was never prescribed. Follow-up mycobacterial blood cultures, inoculated into BACTEC 13A vials, were performed on 9 January, 30 January, 27 February, and 10 April, and all cultures were negative after 12 weeks. As of July 1997, the patient remains well, with no complaints.

Positive blood cultures documented mycobacteremia in this patient, albeit at a low level, indicating disseminated MAC infection. Although intermittent bacillemia has been described early in the course of dissemination, progression is essentially inevitable among patients with late-stage HIV infection [1, 2]. The subsequent absence of any evidence of disseminated MAC over the following 10 months, in the absence of any specific antimycobacterial therapy and concurrent with the markedly increased CD4 cell count (23–245/mm³), suggests that as a result of our patient’s improved immune status, his immune system was able to control the invasive MAC infection. The complete remission of his clinical symptoms and the findings consistent with CMV infection are additional evidence in support of that interpretation.

The effect of new multidrug regimens for the treatment of AIDS, highly active antiretroviral therapy (HAART), on the incidence and course of opportunistic infections (OIs) remains incompletely defined and controversial. Similar to the case we described, there are other reports of cases with remissions of significant OIs in association with intensive antiretroviral therapy and increased CD4 cell counts [3]. However, a recent abstract has indicated that following such treatments, some patients may have the onset of OIs, such as disseminated MAC and CMV retinitis, with “higher than usual CD4 counts” [4, 5], suggesting that the increased number of CD4 cells that appear following HAART may be qualitatively less effective in providing immune resistance.

In summary, we believe that the case we describe is an example of immune control of disseminated MAC disease without antimycobacterial drug therapy in a patient with AIDS whose CD4 cell count increased to >300/mm³ following the institution of combination antiretroviral therapy, including a protease inhibitor.

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Fungemia Due to Hormonema dematioides Following Intense Avian Exposure

Dematiaceous (pigmented) fungi are increasingly recognized as a cause of opportunistic infections in humans [1–7]. Since Lagerberg first described *Hormonema dematioides* [8], one case of infection (a localized skin infection) due to this fungus has been reported [7]. We describe the first case of a systemic infection due to this organism.

In February 1996 a 33-year-old man from Boston who had AIDS (CD4 cell count, 28/mm³) and newly diagnosed Kaposi’s sarcoma presented for a routine visit with a 1-week history of nonproductive cough. He had no other new complaints. His medications, which he took irregularly, included fluconazole for recurrent oral candidiasis (started 3 months before admission); ciprofloxacin, clarithromycin, and ethambutol for *Mycobacterium avium* complex (MAC) bacteremia; and dapsone as prophylaxis for *Pneumocystis carinii* pneumonia (PCP).

The patient had a history of alcoholism, and he had stopped using marijuana and cocaine 2 years previously. He denied any iv drug use. He had never traveled outside the United States or been west of Massachusetts or south of North Carolina. Two years before admission, he had lived for some months in an apartment with a relative who kept 130 uncaged birds, both domestic and wild, including many exotic species; the apartment was littered with bird feces.

On physical examination, the patient did not have fever or dyspnea. Mucocutaneous Kaposi’s sarcoma and oral thrush were present. Auscultation of the chest did not reveal rales or wheezes. A chest radiograph revealed new diffuse reticulonodular infiltrates. His oxygen saturation was 97% while breathing room air. Bronchoscopy was performed; no gross pathological findings were noted. Staining for *Pneumocystis* species and acid-fast bacilli (AFB) was negative. No viral inclusions were seen. Grocott-Go-mori methanamine–silver staining of a bronchial washing specimen revealed intracellular yeasts in pulmonary macrophages, consistent with the appearance of histoplasmosis.

On admission to the hospital 4 days after his clinic visit, the patient was noticeably dyspneic. His temperature was 100°F; his respiratory rate was 24. Findings of the remainder of his physical examination, including his lung examination, were unchanged. His oxygen saturation was 92% while breathing room air. His WBC count was 3,000/mm³ (66% polymorphonuclear cells and 6% bands). His lactate dehydrogenase level was 129 IU/L.

Therapy with iv amphotericin B was started. The patient’s respiratory status was very erratic over the first week. Sometimes his oxygen saturation while breathing room air both before and after exercise was normal, whereas at other times he had bouts of severe dyspnea lasting from hours to days and requiring administration of 100% O₂ by face mask. Parenteral trimetrexate, folinic acid, and corticosteroids were added to the regimen for empirical treatment of PCP. The patient refused to undergo repeated bronchoscopy. Despite therapy, his respiratory status continued to deteriorate, and he died on hospital day 20 of progressive respiratory failure, having received 550 mg of amphotericin B.

Laboratory study results reported post-mortem included respiratory cultures yielding MAC, *Mycobacterium xenopi*, and *Candida albicans*. *Histoplasma* antigen was not detected. Fungal blood cultures performed with use of the Isolator system (Merck & Co., Darmstadt, Germany) yielded a dematiaceous fungus, identified as *H. dematioides* at the University of Texas Health Science Center at San Antonio by methods previously described. The isolate was resistant to fluconazole (MIC, 8μg/mL) but susceptible to amphotericin B (MIC, 0.5 μg/mL).

We describe a patient with AIDS who appears to have developed a lethal infection due to *H. dematioides*—fungemia and pneumoniathe only organism identified [7]. No other primary site of infection was found. (3) Hormonemal infection contributed to our patient’s death. Although other organisms, including those isolated from his respiratory secretions, may have played a pathogenic role, *H. dematioides* was the only organism isolated from his blood. (4) The intense avian exposure was the source of the infection. *H. dematioides* is found in the soil worldwide but has not been recognized previously as a pathogen in birds or other animals.

This case may serve as a warning, particularly with respect to immunocompromised individuals, of the potential danger of altering the accustomed relationship between humans and the natural environment.

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Clinical Infectious Diseases 1998;26:759–60
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