Mycobacterium haemophilum Cellulitis and Osteomyelitis in a Man with AIDS

Karen L. Holladay, MD, and J. Kevin Carmichael, MD

Human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS) have dramatically increased the number of persons living with serious immunosuppression. These persons are at risk for infection by previously uncommon organisms such as *Pneumocystis carinii* and *Mycobacterium avium-intracellulare* complex (MAC). *Mycobacterium haemophilum* is another uncommon organism that is now joining the list of those seen with increasing frequency during the past few years in persons with AIDS.[1-11] *M haemophilum* can cause cellulitis of the extremities, osteomyelitis, arthritis, pneumonia, lymphadenitis, and disseminated disease.[1-16] Definitive identification of *M haemophilum*, following acid-fast staining, requires very specific growth conditions and takes 3 weeks or longer. This requirement can delay diagnosis and proper treatment. We report here a case of *M haemophilum* infection in a person with AIDS that is illustrative of the diagnostic and therapeutic challenges posed by this organism.

Case Report

A 46-year-old man with late AIDS (CD4 < 50) came to a family practice clinic for a regular checkup. He had tested positive for HIV antibodies 2 years previously but had not had any AIDS-defining opportunistic infections diagnosed. He had been a patient at the clinic for 7 months and had recently begun to complain of fatigue, weakness, and occasional fevers and chills. He had chronic pain from an anal fissure and had undergone sphincterotomy. He was taking 5-mg oxycodone tablets four times a day for pain, one trimethoprim-sulfamethoxazole double-strength tablet daily for prophylaxis of *P carinii* pneumonia, 25 mg of amitriptyline for sleep, 100 mg of fluconazole daily to suppress recurrent oral candidiasis, and 250 mg of azithromycin daily for prophylaxis against MAC.

At this visit he casually mentioned pain and swelling of the dorsal surface of his left foot, which had started within the past month. He had no recollection of trauma to the area. The patient was afebrile and only slightly uncomfortable from the pain. Findings on a physical examination were unremarkable. No therapy was instituted, but the patient was instructed to return if his symptoms worsened.

He returned 2 weeks later complaining of increasing pain in the foot. When examined, the patient had a low-grade fever and a swollen, erythematous area about 3 cm in diameter on the dorsal surface of the left foot at the bases of the fourth and fifth metatarsals. He also had a small furuncle on his left elbow. A radiograph of the left foot was obtained, which showed no abnormalities. The patient was prescribed amoxicillin-potassium clavulanate combination, 500 mg three times a day, which was discontinued after 4 days because he developed a rash. Cephalexin 500 mg three times a day was prescribed. The pain and swelling worsened during the following week. A repeat radiograph of the foot was again normal, and a blood culture was negative. The following week, 1 month after the original complaints, the patient had increased swelling of the foot as well as pain and swelling of the right third finger. A third radiograph of the foot revealed soft tissue swelling and a lytic bone lesion in the area of the patient's pain.

Hospital admission was advised, but the patient refused. Several days later the patient telephoned and agreed to admission. At the time of admission both the dorsal aspect of the left foot and the area over the proximal and middle phalanges of his right third finger were erythematous, tender, and fluctuant. The small area of erythema and tenderness on his left elbow had also persisted. He also

Submitted, revised, 12 September 1995.

From the University of Arizona College of Medicine (KLH) and the AIDS Education Programs, Department of Family Medicine, University of Arizona College of Medicine (JKC), and El Rio Special Immunology Associates (JKC), Tucson Arizona. Address reprint requests to J. Kevin Carmichael, MD, El Rio Special Immunology Associates, 445 North Silverbell Road, Suite 202, Tucson, AZ 85745.

complained of pain in the left knee with movement, but it did not appear red or swollen. Incision and drainage were performed on the left foot and right finger lesions. Ten milliliters of purulent material obtained from the foot was sent for Gram stain and culture, acid-fast stain and culture, and fungal stain and culture. Blood was also sent for bacterial and fungal culture and for coccidioidomycosis serologic testing.

Acid-fast stain of the purulent material was strongly positive, and the patient was prescribed antituberculosis therapy with isoniazid 300 mg daily, rifampin 300 mg twice daily, pyrazinamide 500 mg three times daily, and ethambutol 400 mg three times daily. The patient improved slightly on this regimen. Twenty-four days after incision and drainage of the foot lesion, cultures grew only on medium containing X-factor (heme), indicating *M haemophilum*. The patient's medications were changed to ciprofloxacin 750 mg twice a day, rifabutin 300 mg per day, cycloserine 250 mg three times a day, and azithromycin 250 mg twice a day. Two weeks later, the patient's signs and symptoms had markedly improved. Two months later, radiographic findings of the left foot and the right hand were normal.

Discussion

M haemophilum infection remains relatively uncommon but is increasing in frequency. Fifty-four case reports have been published since the first case report in 1978.[17] All the cases occurred in patients who were immunosuppressed or children less than 4 years of age.[1-16] The first case of *M haemophilum* infection in a person with AIDS was reported in 1987;[1] now, more than one half of all published cases have occurred among persons with AIDS. The remaining cases in immunosuppressed patients have occurred in renal and bone marrow transplant recipients and in patients with Hodgkin's disease.[8,9,13-15,17]

Most infections with *M haemophilum* involve the skin. Cases of osteomyelitis, as well as infections of subcutaneous tissues, joints, lungs, lymph nodes, and eye, have also been reported.[1-16] Disseminated infection is fairly common, as evidenced by multiple sites of infection in some patients and positive blood cultures in a few.[2,4,8,9]

Skin lesions occur most commonly on the extremities, but cases involving the face and trunk have also been reported.[3-10,14] In general, the lesions are slow-developing, tender, erythematous, and nodular or vesicular. In most cases, multiple nodules are present,[1-9,14] but in some, only a single nodule appeared.[4,13] Of the cases that describe size of nodules, most are small, 3 cm or less in diameter,[6,9,14] but larger lesions up to 10 cm have also been observed.[11] The color of the lesions varies from erythematous pink or red to dark purple. In some cases the nodules became necrotic and ulcerative.[4,6,9] Drainage from the lesions, whether spontaneous or therapeutic, has been described as serous, serosanguineous, or purulent.

Few cases of *M haemophilum* osteomyelitis have been reported previously. These cases have occurred on the tibiae and fibulae, bilaterally in some cases.[6,7,9,11] The lesions appear lytic on radiographs. As in this patient, the osteomyelitis develops slowly during the course of several weeks.

In those patients with AIDS and *M haemophilum* infection, all CD4 counts were less than 100, and 5 patients had counts of less than 50,[4,6,9,10] as did our patient. The occurrence of previous or concurrent opportunistic infections is variable. Some patients, as ours, had no previous opportunistic infection.[4,6] Others had concurrent *P carinii* pneumonia, Kaposi sarcoma, candidiasis, cryptococcal meningitis, salmonella enteritis, and perianal herpes, or a history of these diseases.

M haemophilum is an acid-fast mycobacterium. It has been shown to form granulomata in some cases[2,6,8,10,13,15,16] and not in others.[4] It is different from *M tuberculosis* because it grows optimally at temperatures 28 to 32 °C, and not at all at 37 °C; this fact has been proposed as an explanation for its growth primarily on the extremities.[4] Also unlike *M tuberculosis*, *M haemophilum* requires heme for growth and does not produce catalase. The exact conditions for optimal culture of *M haemophilum* have been described elsewhere.[18,19] Growth in culture requires at least 3 weeks. Treatment of *M haemophilum* infection has not been standardized. The only constant has been the use of combinations of drugs. In cases where lesions responded to antibiotics, either rifampin or isoniazid or both were used. Other drugs that have been used in successful regimens include pyrazinamide, ethambutol, amikacin, clarithromycin, doxycycline, ciprofloxacin, clofazimine, and minocycline.

This case, as well as most others, shows that treatment of *M haemophilum* infection in AIDS patients is generally efficacious. In most cases, pa-

tients have recovered slowly, taking weeks to months. When *M haemophilum* infection has persisted until the patient died, a concomitant disease was the most likely cause of death.[1,2,6,8,9] A few patients have apparently died from *M haemophilum*; these cases involved serious infections, such as pneumonia,[8,9] and disseminated disease.[9] Other patients, however, have recovered from similar types of infection caused by *M haemophilum*.

In this patient the accurate diagnosis of *M haemophilum* infection took 2 months. After accurate identification of *M haemophilum* and initiation of the appropriate medications, the lesions of his foot, finger, elbow, and knee cleared within 4 weeks. He remained on ciprofloxacin, rifabutin, cycloserine, and azithromycin for 3 months and has had no recurrence of *M haemophilum* infection after 1 year of follow-up care. This case highlights the importance of suspecting unusual infections in persons with HIV infection. Acid-fast bacilli, fungal, and routine bacterial studies of all specimens obtained from patients with HIV infection must be undertaken. The spectrum of pathogens found in these patients is broad and will likely continue to increase as persons with AIDS survive increasingly long periods of time with profound immunosuppression.

References

1. Males BM, West TE, Bartholomew WR. *Mycobacterium haemophilum* infection in a patient with acquired immune deficiency syndrome. J Clin Microbiol 1987;25:186-90.
2. Rogers PL, Walker RE, Lane HC, Witebsky FG, Kovacs JA, Parrillo JE, et al. Disseminated *Mycobacterium haemophilum* infection in two patients with the acquired immunodeficiency syndrome. Am J Med 1988;84:640-2.
3. Thibert L, Lebel F, Martineau B. Two cases of *Mycobacterium haemophilum* infection in Canada. J Clin Microbiol 1990;28:621-3.
4. Kristjansson M, Bieluch VM, Byeff PD. *Mycobacterium haemophilum* infection in immunocompromised patients: case report and review of the literature. Rev Infect Dis 1991;13:906-10.
5. Holton J, Nye P, Miller R. *Mycobacterium haemophilum* infection in a patient with AIDS. J Infect 1991;23:303-6.
6. Dever LL, Martin JW, Seaworth B, Jorgensen JH. Varied presentations and responses to treatment of infections caused by *Mycobacterium haemophilum* in patients with AIDS. Clin Infect Dis 1992;14:1195-200.
7. Gupta I, Kocher J, Miller AJ, Weisholtz SJ, Perz J, Scully M. *Mycobacterium haemophilum* osteomyelitis in an AIDS patient. N J Med 1992; 89:201-2.
8. Kiehn TE, White M, Pursell KJ, Boone N, Tsivitis M, Brown AE, et al. A cluster of four cases of *Mycobacterium haemophilum* infection. Eur J Clin Microbiol Infect Dis 1993;12:114-8.
9. Straus WL, Ostroff SM, Jernigan DB, Kiehn TE, Sordillo EM, Armstrong D, et al. Clinical and epidemiologic characteristics of *Mycobacterium haemophilum*, an emerging pathogen in immunocompromised patients. Ann Intern Med 1994;120:118-25.
10. McGovern J, Bix BC, Webster G. *Mycobacterium haemophilum* skin disease successfully treated with excision. J Am Acad Dermatol 1994;30:269-70.
11. Zuger A. Bone pain in an HIV-infected woman. AIDS Clin Care 1994;6:59-60.
12. Dawson DJ, Blacklock ZM, Kane DW. *Mycobacterium haemophilum* causing lymphadenitis in an otherwise healthy child. Med J Aust 1981;2:289-90.
13. Davis BR, Brumbach J, Sanders WJ, Wolinsky E. Skin lesions caused by *Mycobacterium haemophilum*. Ann Intern Med 1982;97:723-4.
14. Moulsdale MT, Harper JM, Thatcher GN, Dunn BL. Infection by *Mycobacterium haemophilum*, a metabolically fastidious acid-fast bacillus. Tubercle 1983; 64:29-36.
15. Ryan CG, Dwyer BW. New characteristics of *Mycobacterium haemophilum*. J Clin Microbiol 1983;18: 976-7.
16. Armstrong KL, James RW, Dawson DJ, Francis PW, Masters B. *Mycobacterium haemophilum* causing perihilar or cervical lymphadenitis in healthy children. J Pediatr 1992;121:202-5.
17. Sompolinsky D, Lagziel A, Naveh D, Yankilevitz T. *Mycobacterium haemophilum* sp. nov., a new pathogen of humans. Int J Syst Bacteriol 1978;28:67-75.
18. Sompolinsky D, Lagziel A, Rosenberg I. Further studies of a new pathogenic mycobacterium (*M. haemophilum* sp. nov.). Can J Microbiol 1979;25: 217-26.
19. McBride JA, McBride ME, Wolf JE Jr. Evaluation of commercial blood-containing media for cultivation of *Mycobacterium haemophilum*. Am J Clin Pathol 1992; 98:282-6.