Fernando García-Garrote[1], *María Jesús Ruiz-Serrano*[1], *Jaime Cosín*[1], *Luis Alcalá*[1], *Arturo Ortega*[2], *Emilio Bouza*[1]
[1]Department of Microbiology and Infectious Diseases, Hospital General Universitario 'Gregorio Marañón', Madrid, Spain; [2]Mycobacteriology Reference Laboratory, Instituto de Salud Carlos III, Madrid, Spain

Accepted 17 May 1997

References

1. Havlik JA, Horsburgh CR, Metchock B, Williams PP, Fann SA, Thompson SE III. Disseminated *Mycobacterium avium* complex infection: clinical identification and epidemiologic trends. J Infect Dis 1992; 165: 577–80.
2. Piersimoni C, Tortoli E, De Sio G. Disseminated infection due to *Mycobacterium celatum* in patient with AIDS. Lancet 1994; 344: 332.
3. Bouza E, Diaz-Lopez MD, Moreno S, Bernaldo de Quiros JCL, Vicente T, Berenguer J. *Mycobacterium tuberculosis* bacteremia in patients with and without human immunodeficiency virus infection. Arch Intern Med 1993; 153: 496–500.
4. Butler WR, O'Connor SP, Yakrus MA, et al. *Mycobacterium celatum* sp. nov. Int J Syst Bacteriol 1993; 43: 539–48.
5. Tortoli E, Piersimoni C, Bacosi D, et al. Isolation of the newly described species *Mycobacterium celatum* from AIDS patients. J Clin. Microbiol 1995; 33: 137–40.
6. Piersimoni C, Tortoli E, de Lalla F, et al. Isolation of *Mycobacterium celatum* from patients infected with human immunodeficiency virus. Clin Infect Dis 1997; 24: 144–7.
7. Bull TJ, Shanson DC, Archard LC, Yates MD, Hamid ME, Minnikin DE. A new group (type 3) of *Mycobacterium celatum* isolated from AIDS patients in the London area. Int J Syst Bacteriol 1995; 45: 861–2.
8. Zurawski CA, Cage GD, Rimland D, Blumberg MH. Pneumonia and bacteremia due to *Mycobacterium celatum* masquerading as *Mycobacterium xenopi* in patients with AIDS: an underdiagnosed problem? Clin Infect Dis 1997; 24: 140–3.
9. Haase G, Skopnik H, Batge S, Bottger EC. Cervical lymphadenitis caused by *Mycobacterium celatum*. Lancet 1994; 8: 344: 1020–1.
10. Butler WR, O'Connor SP, Yakrus MA, Gross WM. Cross-reactivity of genetic probe for detection of *Mycobacterium tuberculosis* with newly described species *Mycobacterium celatum*. J Clin Microbiol 1994; 32: 536–8.
11. Kent PT and Kubica GP. Public Health Mycobacteriology: A guide for the level III laboratory. US Department of Health and Human Services Publications 1986; 8230: 71–157. Atlanta, CDC.

Recovery of *Mycobacterium haemophilum* skin infection in an HIV-1-infected patient after the start of antiretroviral triple therapy

Clin Microbiol Infect 1997; 3: 584–585

A 30-year-old caucasian HIV-1-infected woman with a history of *Pneumocystis carinii* pneumonia presented with multiple painful cutaneous nodules on the extremities. Her $CD4^+$ T-cell count was 50/mm^3. She had recently returned from the island of St Maarten, where she had lived for 4 years. Her medication included cotrimoxazole 480 mg once daily as PCP prophylaxis, and zidovudine 200 mg three times daily with zalcitabine 0.75 mg three times daily as antiretroviral therapy. Physical examination revealed tender, erythematous nodular lesions on the extremities, especially overlying the knee, the first metatarsal and elbows. A few ulcerative lesions discharged purulent material. Microscopic examination of biopsy specimens revealed a purulent inflammatory reaction with many acid-fast bacilli. A *Mycobacterium marinum* skin infection was suspected and the skin lesions resolved subsequent to treatment with doxycycline 200 mg once daily for two months.

Two weeks after discontinuation of doxycycline, however, the skin lesions relapsed and rapidly progressed despite retreatment with doxycycline. A second biopsy was performed and *Mycobacterium haemophilum* was identified using a nested PCR of 16S rRNA gene fragments followed by direct sequence determination [1]. Cultures of the skin biopsy on Middlebrook 7H11 medium supplemented with 60 μmol hemin revealed *M. haemophilum* after 3 weeks of incubation at 30°C. Antibiotic susceptibility tests were not performed. The skin lesions failed to respond to treatment with ciprofloxacin 750 mg twice daily, rifampin 600 mg once daily and clarithromycin 500 mg twice daily for 8 weeks, and progressed further despite a change of therapy to minocycline 100 mg once daily, rifabutin 300 mg once daily and ethambutol 15 mg per kg once daily. New mutilating skin lesions developed in the face and in the right flexor side of the knee. Therefore, the regimen was changed to isoniazid 300 mg once daily, ciprofloxacin 750 mg twice daily and cycloserine 250 mg twice daily, and antiretroviral therapy was altered simultaneously to triple therapy of stavudine (d4T) 30 mg twice daily, lamivudine (3TC) 150 mg twice daily and indinavir 800 mg three times daily. The patient's condition improved remarkably and the skin lesion slowly healed with formation of scars. After 2 months of treatment, all ulcerating skin lesions had disappeared except for a residual lesion in the knee. A reduction in the number of plasma HIV RNA copies from 12 000 copies per mL to values below the detection limit (1000 copies per mL, NASBA-QT;

ORGANON, TEKNIKA, Boxtel, The Netherlands) and an increase of the cell-mediated immunity as reflected by an amelioration of T-cell stimulation tests with CD3 monoclonal antibodies (3–40% in comparison with the response in healthy controls) was observed. The $CD4^+$ T-cell count had been modestly increased from 50/mm^3 to 70/mm^3.

M. haemophilum, the 'blood-loving mycobacterium', was first described in 1978 as a cause of subcutaneous infection in a patient with Hodgkin's disease [2]. *M. haemophilum* causes cutaneous lesions (similar to the related *M. marinum* and *M. ulcerans*), arthritis, and pulmonary infections in immunocompromised patients [3]. These cutaneous lesions are most often found on the extremities, especially overlying the joints, and are not sporotrichoid in appearance. Of 64 cases of *M. haemophilum* infections reviewed recently, 53 have been reported in immunocompromised adults, nine have been reported in children, primarily as localized lymphadenitis in the cervical region or perihilar lymphadenitis, and two have been reported in adults whose risk factors were not known [3]. Culture-proven *M. haemophilum* infections in immunocompetent adults have not been reported. The most frequent underlying diseases associated with *M. haemophilum* infections were AIDS, renal transplant recipients, bone marrow transplant recipients, lymphoma, and rheumatoid arthritis.

The natural habitat of *M. haemophilum* is unknown and attempts to recover it from environmental samples have been unsuccessful. The geographic distribution of reported *M. haemophilum* cases suggests that the bacterium is ubiquitous but the means of acquisition of the organism remain unknown, even when clustering of cases occur [4,5].

There are no standardized methods for antimicrobial susceptibility testing of *M. haemophilum*. A variety of agar methods and a broth microdilution method have been described in the case reports. One study reports on a larger number of isolates (n=17) which were tested using a modification of a microdilution broth method [6]. Ethambutol, tetracycline and trimethoprim–sulfamethoxazol were inactive against *M. haemophilum*, whereas isoniazid was weakly active and ciprofloxacin, ofloxacin and sparfloxacin showed moderate activity. The most active antimicrobial agents were clarithromycin and rifabutin. Additionally, combined rifabutin and clarithromycin provided effective treatment for experimentally induced disseminated *M. haemophilum* infection in immunocompromised mice [7].

Twenty-nine of the approximately 60 cases of *M. haemophilum* infection reported worldwide were diagnosed in HIV-1-infected individuals who appeared to have a strong immunodeficiency ($CD4^+$ count <50/mm^3). In only six of these 29 patients did skin lesions resolve after the initiation of antimycobacterial therapy. The contribution of antibiotics to the healing of *M. haemophilum* lesions is difficult to evaluate. Recovery from *M. haemophilum* infections may depend mostly on an improvement of the immunologic state or surgical drainage [8]. Our observation in this patient suggests that, in addition to antimycobacterial antibiotic treatment, improvement of the cell-mediated immunity induced by antiretroviral triple therapy contributes considerably to the recovery from a persistent *M. haemophilum* skin infection.

E. J. Kuijper[1], *F. W. N. M. Wit*[2], *J. Veenstra*[2], *E. C. Böttger*[3]
[1]Department of Medical Microbiology, Academic Medical Centre, Amsterdam, The Netherlands;
[2]Department of Infectious Diseases, Tropical Medicine and AIDS, Academic Medical Centre, Amsterdam, The Netherlands;
[3]Institut für Medizinische Mikrobiologie, Medizinische Hochschule, Hannover, Germany

Accepted 19 May 1997

References

1. Emler S, Böttger EC, Broers B, Cassis I, Perrin L, Hirschel B. Growth deficient mycobacteria in patients with AIDS: diagnosis by analysis of DNA amplified from blood or tissue. Clin Infect Dis 1995; 20: 772–5.
2. 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.
3. Saubolle MA, Kiehn TE, White MH, Rudinsky MF, Armstrong D. *Mycobacterium haemophilum*: microbiology and expanding geographic spectra of disease in humans. Clin Microbiol Rev 1996; 9: 435–47.
4. Kiehn TE, White M, Pursell KJ, et al. A cluster of four cases of *Mycobacterium haemophilum* infection. Eur J Clin Microbiol Infect 1993; 12: 114–18.
5. Gouby A, Branger B, Oules R, Ramuz M. Two cases of *Mycobacterium haemophilum* infection in a renal-dialysis unit. J Med Microbiol 1988; 25: 299–300.
6. Bernard EM, Edwards FF, Kiehn TE, Brown ST, Armstrong D. Activities of antimicrobial agents against clinical isolates of *Mycobacterium haemophilum*. Antimicrob Agents Chemother 1993; 37: 2323–6.
7. Atkinson BA, Bocanegra R, Graybill JR. Treatment of *Mycobacterium haemophilum* infection in a murine model with clarithromycin, rifabutin, and ciprofloxacin. Antimicrob Agents Chemother 1995; 39: 2316–19.
8. Branger B, Gouby A, Oules R, et al. *Mycobacterium haemophilum* and *Mycobacterium xenopi* associated infection in a renal transplant patient. Clin Nephrol 1985; 23: 46–9.