Disseminated *Mycobacterium avium* Complex In An Immunocompetent Previously Healthy Woman

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Mycobacterium avium complex (MAC) has become in certain regions more commonly isolated than *M. tuberculosis*. The number of reported cases has increased secondary to the acquired immunodeficiency syndrome (AIDS), yet knowledge is limited about its transmission or process of infectivity. Disseminated disease usually had been associated with severe underlying diseases, such as AIDS, immune system anomalies, and lymphoma; however, the number of cases in which there is no predisposing condition is growing. Reported here is a case of disseminated MAC infection with multiple sites of involvement in a woman who had no predisposing disease. A discussion of the disease process of MAC infection is also presented. This case highlights many of the problems associated with MAC disease, including delay in diagnosis, the undefinable mode of transmission, the potential severity of the disease, and the difficulty in treatment.

Case Report

A 31-year-old woman from rural North Carolina sought care at a suburban community hospital for severe thoracic back pain. She stated that the pain had been increasing in intensity during the previous 5 weeks. Her medical history was notable for multiple treatments for pneumonia, upper respiratory tract infections, and thoracic musculoskeletal strain during the previous 2 years. She had received both oral and intravenous antibiotics for the presumptive diagnosis of community-acquired pneumonia and had been admitted to the hospital on three occasions. (On one occasion she required ventilatory assistance secondary to respiratory failure and underwent bronchoscopy for diagnosis during that intubation.) She had received nonsteroidal anti-inflammatory therapy intermittently during that same period for her complaints of vague chest discomfort. She had several sputum cultures, three human immunodeficiency virus tests, multiple serum analyses, and cultures of blood, sputum, and bronchoscopic specimens, which were all negative for pathogens. She had several chest radiographs showing infiltrates, which prompted the above interventions, but follow-up films were performed only once, showing clearing of the infiltrate.

Three months before her current back pain complaints, the patient developed a 5.0-cm nontender immobile axillary mass and a 3.0-cm tender, immobile sternal mass. Aspirations were done on thick-walled abscesses and sent for culture. Because of concomitant complaints of back pain, spinal films were performed, which showed a large paraspinal mass. This mass was aspirated and cultured as well. All cultures were positive for acid-fast bacillus and the patient was given isoniazid, pyridoxine, and rifampin, as well as clarithromycin for the presumptive diagnosis of tuberculosis. The definitive typing, however, was *M. avium* complex infection, and the tuberculous therapy was discontinued. At this time, the patient was lost to follow-up as result of noncompliance and poor communication.

The patient subsequently appeared at our institution and had cultures done on the large paravertebral abscesses, now destroying the vertebral bodies of T7 and T8, as well as the sternal abscess, which was draining a purulent material. These cultures were also typed as acid-fast bacillus and eventually as *M. avium* complex infection. The patient's hospital course consisted of implementation of antimycobacterial therapy, evaluation and treatment of the skeletal complaints, and investigation of her immune status. The patient was started on a regimen of ciprofloxacin 750 mg twice a day, clarithromycin 500 mg twice a day, rifampin 600 mg daily, and ethambutol 400 mg twice a day. Cycloserine 250 mg three times a day was added during her hospitalization. A bone scan revealed multiple sites of metastatic osteo-

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myelitis, including the proximal femurs, distal radius, vertebral bodies of T7 and T8, the sternum, and the pelvis. Results of computed tomographic scans of the head, thorax, and abdomen were normal. A complete blood count, a CD4 count, an angiotensin converting enzyme level, T-cell subset studies, cerebrospinal fluid from lumbar puncture, echocardiogram, HIV testing, and sputum and blood cultures were within normal limits. The patient gradually improved and was discharged to a rehabilitation hospital. She was expected to continue taking ciprofloxacin, clarithromycin, rifampin, ethambutol, and cycloserine for at least 2 years.

Discussion

M. avium-intracellulare is a nontuberculous mycobacteria that was not considered a human pathogen until the 1950s. Since then, it has been so recognized and is increasing to such an extent that in some areas of the country it has replaced *M. tuberculosis* in the frequency of reported cases.[1-5] Technically, the two very similar mycobacteria, avium and intracellulare, are considered collectively and termed *M. avium* complex.[1,6] *M. avium-intracellulare* was described in the now defunct Runyon Classification System as a group III.[1,3,5] The organism is highly pathogenic in chickens, swine, and cattle.[1,3-5] The organism is ubiquitous in nature and has been isolated from soil, water, milk, animals, birds, and foodstuffs.[1,5-7] These organisms are highly resilient and have been shown to survive in the soil for up to 4 years.[1]

Much is known about the behavior of these organisms in the environment and in vitro; however, very little is known about the process of infectivity to man in vivo.[1-5,7] There is little concrete evidence to indicate any one method of transmission.[1,4,5,7,8,9] Human-to-human transmission is a possibility but is not considered a probability.[5,8] The epidemiologic evidence indicates that the organisms are widespread in rural southeastern and rural northeastern United States[1,3,4,7,10]; however, no consistent exposure to animals, birds, or infected soil has been implicated as the mode of transmission. In a large study of 1293 patients, 577 (44 percent) were female, 131 (10 percent) were African-American, 372 (29 percent) were from rural areas, and only 36 (3 percent) were between the ages of 15 and 29 years.[8] In this case, the patient had no contact with any known human MAC carriers. She was from the rural southeast but had no other known risk factors for the development of disseminated MAC disease, and she was previously healthy. There has been one report of a MAC epidemic where the causative agent was an infected bronchoscope.[11] Notwithstanding, this case demonstrates the inability to define concretely the source of most MAC cases in immunocompetent patients.

It had been originally thought that a MAC infection implied immunosuppression or a compromised host, because the finding of MAC infection was rare in the immunocompetent patient.[1-7,12,13] Most of the patients with disseminated disease have had discernible abnormalities of cellular-mediated immunity.[8] The numbers of MAC patients without predisposing conditions, however, have been increasing as well, thus indicating a possible change in the pattern of the disease process.[6,7,14] Because a large inoculum is required for the dissemination of the disease, as suspected by the extent of tissue involvement, and a noncasual source is suspected to be the initiator of the disease process, we are challenged to find not only the mechanism of infectivity but the change in virulence that would account for the increased number of cases reported. This case highlights the need for a heretofore nonexistent large-scale study of patients without predisposing factors who become infected with disseminated MAC disease.[3,15] Approximately 24 to 46 percent of persons with pulmonary disease caused by MAC infection are apparently healthy women who have no evidence of predisposing factors.[16]

Regardless of exactly how the organism is transmitted, the spread of the disease in vivo seems to be homogeneous.[1,3] Once an immunocompetent host is infected, the disease process will most likely involve the pulmonary, genitourinary, or skeletal systems. Histologically, the offending process is a nonspecific inflammatory and granulomatous change with or without necrosis.[1,6,7,17] *M. avium-intracellulare* is an intracellular bacterium that multiplies within phagocytic cells.[18] There is a loose aggregation of mononuclear cells, epithelioid cells, and nuclear debris.[7] The local tissue destruction of the parasternal and paravertebral abscesses found in this patient was typical of these lesions, which are similar to those caused by *M. tuberculosis* in the destruction of skeletal tissues.[1,6] There has been

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one reported case of paraspinous MAC abscess with destruction of the local tissues similar to that seen in this case report.[4]

The most common symptoms on presentation are fever (54 percent), weight loss (32 percent), local pain (32 percent), cough (22 percent), night sweats (14 percent), and chills (11 percent). The most common signs of infection have been fever (54 percent), lymphadenopathy (43 percent), hepatomegaly (43 percent), and splenomegaly (35 percent).[4,7,17] These indicators are relatively nonspecific, however, and there is no specific indicator of infection. The reference standard in diagnosis remains positive culture. This would explain why the diagnosis of disseminated MAC disease has been difficult, elusive, and often confused with such malignancies as Hodgkin disease or lymphoma.[2,17] Radiologic evidence might not become evident for 2 to 3 years after initial infection.[3] The delay in diagnosis has resulted in the protraction of symptoms on the average from 25.6 to 36.5 weeks with the length of time from onset of symptoms to diagnosis of 5.3 months.[3,7] Again, the above case is consistent with these data, for not only did the patient's true diagnosis escape definitive conclusion, but even through the multiple investigations of pneumonia, there was little radiologic evidence to assist in diagnosis.

The treatment of focal and disseminated MAC disease remains quite difficult, in large part because of the ability of the organism itself to develop resistance to antimicrobial agents.[3,5,6] Since the publication of the original treatment guidelines in 1985 by Iseman, et al.,[8] there have been many changes in therapy recommendations.[12,16] Heifets, et al.[10] have broken down the symptom complex into categories with treatment recommendations, and there are treatment protocols that have been successful.[4,6,7,9,12,13,16] Responders to therapy originally received on the average 4.8 (± 0.4) drugs, while those failing therapeutic intervention received 2.5 (± 0.6) drugs.[4,7,9,12,16] Most regimens include rifampin, ethambutol, ciprofloxacin, and cycloserine. Horsburgh found that MAC disease without AIDS was most responsive to combinations involving cycloserine.[7] Most recently and very promising is the development of the macrolide clarithromycin, which has been shown to be bacteriocidal toward MAC disease by disruption of intracellular growth and decreasing the amount of bacteria in blood samples.[8,10,18-20] MAC disease is difficult to treat because the bacteria are capable of developing resistance quite readily.[3,8,17] Also because the complex multiplies intracellularly, the minimum inhibitory concentrations are not sufficient to predict the in vivo efficacy of the agents being tested.[18] Disseminated disease obviously requires more aggressive therapy, meaning both multiple drug regimens and extended treatment times.[8]

References

1. Kwong JS, Munk PL, Connell DG, Dianoulis ME. Case report 687. Disseminated *Mycobacterium avium-intracellulare* osteomyelitis. Skeletal Radiol 1991; 20:458-62.
2. Bender BL, Yunis EJ. Disseminated nongranulomatous *Mycobacterium avium* osteomyelitis. Hum Pathol 1980; 11:476-8.
3. Prince DS, Peterson DD, Steiner RM, Gottlieb JE, Scott R, Israel HL, et al. Infection with *Mycobacterium avium* complex in patients without predisposing conditions. N Engl J Med 1989; 321:863-8.
4. O'Brien RJ, Geiter LJ, Snider DE Jr. The epidemiology of nontuberculous mycobacterial diseases in the United States. Results from a national survey. Am Rev Respir Dis 1987; 135:1007-14.
5. O'Brien RJ. The epidemiology of nontuberculous mycobacterial disease. Clin Chest Med 1989; 10: 407-18.
6. Brodkin H. Paraspinous abscess with *Mycobacterium avium-intracellulare* in a patient without AIDS. South Med J 1991; 84:1385-6.
7. Horsburgh CR Jr, Mason UG 3d, Farhi DC, Iseman MD. Disseminated infection with *Mycobacterium avium-intracellulare*. A report of 13 cases and a review of the literature. Medicine 1985; 64:36-48.
8. Iseman MD, Corpe RF, O'Brien RJ, Rosenzweig DY, Wolinsky E. Disease due to *Mycobacterium avium-intracellulare*. Chest 1985; 87(2;Suppl)139S-149S.
9. Mehta JB, Morris F. Impact of HIV infection on mycobacterial disease. Am Fam Physician 1992; 45: 2203-11.
10. Heifets LB, Lindholm-Levy PJ, Comstock RD. Clarithromycin minimal inhibitory and bacteriocidal concentrations against *Mycobacterium avium*. Am Rev Respir Dis 1992; 145:856-8.
11. Gubler JG, Salfinger M, von Graevenitz A. Pseudoepidemic of nontuberculous mycobacteria due to a contaminated bronchoscope cleaning machine. Report of an outbreak and review of the literature. Chest 1992; 101:1245-9.
12. Davidson PT. The diagnosis and management of disease caused by *M. avium* complex, *M. kansasii*, and other mycobacteria. Clin Chest Med 1989; 10:431-43.
13. Sathe SS, Reichman LB. Mycobacterial disease in patients infected with the human immunodeficiency virus. Clin Chest Med 1991; 10:445-63.

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14. Nassos PS, Yajko DM, Sanders CA, Hadley WK. Prevalence of *Mycobacterium avium* complex in respiratory specimens from AIDS and non-AIDS patients in a San Francisco hospital. Am Rev Respir Dis 1991; 143:66-8.
15. Reich JM. Primary pulmonary disease due to *Mycobacterium avium-intracellulare*. Chest 1992; 101:1447-8.
16. Cook JL. *M. avium*, the modern epidemic. Medical/Scientific Update 1992; 10:1-3.
17. Woods GL, Washington JA 2d. Mycobacteria other than *Mycobacterium tuberculosis*: review of microbiologic and clinical aspects. Rev Infect Dis 1987; 9:275-94.
18. Perrone C, Gikas A, Truffot-Pernot C, Grosset J, Pocidalo JJ, Vilde JL. Activities of clarithromycin, sulfisoxazole, and rifabutin against *Mycobacterium avium* complex multiplication within human macrophages. Antimicrob Agents Chemother 1990; 34:1508-11.
19. Ruf B, Schurmann D, Mauch H. Acquired resistance of MAI to clarithromycin. Am Rev Respir Dis 1992; 101:1447-8.
20. Dautzenberg B, Truffot C, Legris S, Meyohas MC, Berlie HC, Mercat A, et al. Activity of clarithromycin against *Mycobacterium avium* infection in patients with acquired immunodeficiency syndrome. A controlled clinical trial. Am Rev Resp Dis 1991; 144:564-9.

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