Disseminated Nocardia otitidiscaviarum in a patient with AIDS

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CASE PRESENTATION

A 59-year-old Caucasian man, diagnosed as HIV-1 positive two years prior, previously asymptomatic and antiretroviral naive, presented in July 1995 with a three-week history of weight loss, fever, night sweats, dyspnea, productive cough and an enlarging mass in his left upper abdominal quadrant and left chest wall. The patient’s chest had sustained no local penetrating trauma. He had returned from the west coast of Africa, where he had resided since 1989, because of his illness.
Past medical history included smoking, past malaria, remote alcohol abuse and shingles in 1990. There was no history of tuberculosis, positive tuberculin skin tests, syphilis, gonorrhea, chlamydia, malignancies or hepatitis. His HIV risk factors included heterosexual contacts in Africa.

Physical examination revealed a thin cachectic man, hemodynamically stable with a low grade fever. Pertinent findings included oral thrush and a large protuberant mass over his left upper abdominal quadrant and left chest wall which was tender to palpation and fluctuant (Figure 1). Chest auscultation revealed coarse crepitations bilaterally at the bases, with dullness to percussion of the left base. Large bilateral non-tender mobile axillary lymph nodes were palpable. Neurological examination was normal.

Investigations revealed a white blood cell count of $11.3 \times 10^9/L$, hemoglobin 101 g/L, platelet count $641 \times 10^9/L$ and CD4 lymphocyte count 206 cells/mm$^3$. Chest radiograph revealed ill-defined masses in the left lung and a consolidation in the left costophrenic angle and pleura. Faint nodules were also evident in the right lung. Augmented computed tomography revealed large separted extraperitoneal mass crossing both inside and outside the left thoracic and abdominal wall, and extending down to the iliac crest (Figure 2).

Percutaneous aspiration of the mass produced thick green fluid revealing abundant beaded branching Gram-positive bacilli on Gram stain; these bacteria were also detected in sputum samples. Further identification revealed *N. otitidiscaviarum*.

*N. otitidiscaviarum* was initially identified by Gordon techniques as outlined by Mishra et al (4) and Lechevalier (5). Direct microscopy for nocardial filamentation was done on four-day-old cultures grown in slide cultures on Sabouraud glucose agar and pyruvate-yeast extract agar (6,7), a specialized medium promoting aerial filamentation in aerobic actinomycetous organisms. In addition, cellular fatty acid constituents were assayed with the MIDI gas-liquid chromatography system (Microbial ID Inc, Delaware).

The organism produced acid from arabinose, glucose, glycerol, inositol and galactose, but not adonitol, cellobiose, erythritol, lactose, maltose, mannitol, melezitose, alpha-methyl-D-glucoside, raffinose, rhamnose, sorbitol, trehalose, dulcitol, sucrose, melibiose and inulin. It cleared suspended xanthine solids but not casein, tyrosine or adenine. It was urease positive. Visible orange carotenoid pigments were seen in cultures. Bromersol purple-milk solids-glucose agar was alkalinized without clearing of milk solids. In chromatography of fatty acid methyl esters, the organism possessed the signature tuberculostearic acid distinguishing nocardioforms from *Streptomyces* species and many other comparable filamentous aerobic actinomycetes (5). The MIDI databases available at the time (August 1995, TSBA Revision 3.80, CLIN Revision 3.80) did not find a match for the fatty acid profile. Species identification was based on Gordon characters, which were unambiguously characteristic of *N. otitidiscaviarum*.

Susceptibility testing was done by the modified Kirby-Bauer disk diffusion methods of Wallace et al (8) and Wallace and Steele (9). Standardized inoculum was prepared by grinding colonies scraped from the surface of Sabouraud peptone-glucose agar plates to a fine slurry in a glass tissue grinder with sintered pestle and tube interior. The homogenized inoculum was then diluted with reference to a 0.5 McFarland barium sulfate standard and streaked evenly on Mueller-Hinton agar. Control isolate ATCC 19247 was used as recommended by Wallace and Steele (9). Only tests where the control’s inhibition zone size
was within the specified range were read for the test organism. Results showed that the organism gave susceptible values for amikacin and trimethoprim/sulfamethoxazole (TMP/SMX), although the zone size for the latter was near the borderline. Resistance was shown to cefotaxime, tobramycin, gentamicin, minocycline and erythromycin. Certain drugs without published breakpoints for nocardiae were tested for taxonomic reasons or to supply a rough estimate of relative responsiveness in case of extreme clinical urgency. The organism was completely resistant to cefamandole and streptomycin (no zone) and had a moderately wide zone size for imipenem (39 mm).

Following surgical drainage and debridement of the abscess, the patient deteriorated with rapid widespread pulmonary involvement (Figure 3) requiring intubation and ventilation in the intensive care unit. Initial medical therapy consisted of TMP/SMX (160 mg TMP, 800 mg SMX) parenterally every 6 h and amikacin 500 mg parenterally every 12 h, for six weeks. Initial treatment also included parenteral cefotaxime. He responded well to treatment and eventually was discharged from the hospital and was initially maintained on nontoxic therapy with zidovudine and zalcitabine.

**DISCUSSION**

Nocardiosis in patients with HIV infection is probably under-recognized and not as rare as previously suspected (10). In previous reports of nocardiosis due to *N. asteroides* in AIDS patients, the incidence rate was 1.8% (1), higher than the rate of 0.2% to 0.3% previously reported by the Centers for Disease Control and Prevention, Atlanta, Georgia (11). The majority of pulmonary and extrapulmonary cases of nocardia in AIDS patients have involved *N. asteroides* (1,2,12-15), *N. brasiliensis* (3) or *Nocardia farcinica* (14,15), and most frequently involved the lung (51.7%) and brain (11.7%) in one series (10). There are six forms of disease recognized in humans: pulmonary; systemic or disseminated; central nervous system; extrapulmonary; cutaneous or lymphocutaneous; and actinomycetomas (10). Large abscesses enlarge by progressive extension of filaments into the tissue and may behave like a bacterial abscess (10). The mortality rate due to nocardiosis was 65% in one series and largely attributed to disseminated infection, relapse of infection and severe immunosuppression (1). *N. otitidiscaviarum*, however, is rarely reported as a cause of infection in patients with AIDS, described in only scattered case reports (14,16,17).

*N. otitidiscaviarum* is a soil saprophyte with worldwide distribution and an infrequent cause of mycetomas in humans (10). Disseminated infection in humans has been reported in the pre-AIDS era in patients immunocompromised by underlying malignancy or corticosteroids (18).

This report describes a case of disseminated infection due to *N. otitidiscaviarum* according to previously defined criteria (10). Despite the high morbidity and mortality reported in previous series (1), the patient responded well to aggressive surgical drainage and parenteral antibiotics with long term suppressive therapy with TMP/SMX. The patient described had an initial CD4 lymphocyte count of 206 cells/mm³ at presentation, higher than the mean CD4 lymphocyte count of 109 cells/mm³ in the previous series (1). Antimicrobial susceptibility testing of *Nocardia* species has been problematic because of a lack of standardization in methodology. However, optimal drug selection will depend on antimicrobial susceptibility because of drug resistance patterns and often the need for long term therapy (19). The *N. otitidiscaviarum* isolate in this case was susceptible to amikacin and TMP/SMX.

The optimal therapy for nocardiosis has yet to be determined; however, the use of TMP/SMX is a mainstay of therapy with approximately 80% of patients initially responding in one series (1). The patient described remains on long term suppressive therapy with TMP/SMX, which appears to be necessary to prevent relapse in patients with advanced HIV infection (1,2), and likely protects patients from primary infection with nocardia. Nocardia are opportunistic organisms causing serious infections in HIV-infected patients and are associated with a high mortality. Nocardiosis is likely under-recognized, and consideration should be given to adding this infection to AIDS-defining conditions in adults.

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**REFERENCES**


**CLINICAL VIGNETTE**

Continued from page 322

**DIAGNOSIS**

The organism grew on both 5% sheep blood agar and Sabouraud’s dextrose agar only when overlaid with olive oil. Creamy yeast-like colonies grew within 72 h and were identified as Malassezia furfur. The infusion port was removed, and the patient was treated with amphotericin B to a total dose of 15 mg/kg. Susceptibility testing was not performed. The patient became afebrile after five days of treatment and has remained free of disease for six months.

**DISCUSSION**

*M. furfur* is perhaps best known as the cause of tinea versicolor; however, it also causes central venous catheter infections in neonates and rarely in adults. Adults tend to present with fever and have immunosuppression or severe underlying disease, which is usually gastrointestinal in nature (1). There is a significant association with intravenous lipid administration; however, adult cases have recently been reported where this has not been so (2,3). *M. furfur* is a lipophilic yeast requiring long chain fatty acids for optimal growth, explaining why it does not grow on most mycological media without supplementation. Treatment consists of discontinuing lipids, removing the central venous catheter and administering systemic antifungal agents. Although administering amphotericin B through the central line has not provided effective treatment, success with antibiotic lock therapy has recently been described (4). Amphotericin B and heparin are instilled into the central venous catheter which is then locked for 12 h daily for 21 days. Prospective validation of this method is currently lacking. The diagnosis of *M. furfur* should be entertained in any adult who has fever and a central venous catheter in the presence of serious comorbid illness or intravenous lipid administration.

**REFERENCES**

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