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Fatal Pulmonary *Nocardia farcinica* Infection

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***Nocardia farcinica* infections are rare and potentially life threatening. Identification is based on growth at 45°C, opacification of Middlebrook 7H10 agar, and resistance to antibiotics. We describe a case of fatal pulmonary *N. farcinica* infection in a patient with pneumoconiosis that was diagnosed by culture of sputum onto selective media.**

Nocardiosis is a rare and potentially life-threatening infection caused by several species of the genus *Nocardia. Nocardia asteroides* complex and *Nocardia brasiliensis* are the species most frequently involved in human disease. In 1888 Nocard isolated an actinomycete from cows with bovine farcy in Guadeloupe, and this strain was characterized and named *Nocardia farcinica*. In 1962 Gordon and Mihm described an identification scheme that could not distinguish Nocard's initial isolate from strains of *N. asteroides*, and thus, they grouped the two together (6). Later, Wallace and Tsukamura demonstrated that this organism, together with other isolates, formed an independent species distinct from *N. asteroides* (11, 12), which has recently been redefined as a separate species, *N. farcinica*. Identification of *N. farcinica* is important because of its aggressiveness, its tendency to disseminate, and its resistance to antibiotics (10, 12). Herein we describe a case of fatal pulmonary nocardiosis caused by *N. farcinica* in a 77-year-old patient with pneumoconiosis but no other predisposing factors and which was diagnosed by means of culture of expectorated sputum.

Case report. A 77-year-old male was seen in the emergency department for evaluation of a 6-day history of severe dyspnea, nonproductive cough, and low-grade fever. He had worked as a coal miner and had mild pneumoconiosis. He had previously been mostly healthy and had never received steroid treatment. On admission, physical examination revealed a temperature of 37.6°C and a respiration rate of 30; basal crackles were audible in the left lung. Laboratory studies performed on admission revealed a hemoglobin level of 126 g/liter, a leukocyte count of 17.8×10^9/liter (with 91.4% polymorphonuclear cells, 5.7% monocytes, and 2.5% lymphocytes). Arterial blood gases revealed a pH of 7.51, a partial O_2 pressure of 49.2 mm Hg, and a partial CO_2 pressure of 32.4 mm Hg. Chest radiography showed left middle and lower lobe infiltrates. A diagnosis of bacterial pneumonia was established, and treatment with intravenous cefotaxime (1 g four times a day) and prednisone was initiated. A sputum specimen was rejected for culture because of the presence of >10 squamous epithelial cells per low-power field; acid-fast smears and mycobacterial cultures (three samples) were negative, and blood cultures yielded no growth. Over the next 15 days, the patient's fever and productive cough persisted; a repeated chest radiograph revealed extensive left lower lobe infiltrate. Cefotaxime was discontinued, and intravenous piperacillin/tazobactam (2 g four times a day) was prescribed. Direct examination of a Gram-stained smear of a new sputum specimen revealed <10 squamous epithelial cells and >25 leukocytes per ×100 field and numerous gram-positive branching rods suggestive of *Nocardia* species. Sputum was inoculated onto Thayer-Martin and selective buffered charcoal yeast extract (BCYE) containing anisomycin, polymyxin, and vancomycin media and was incubated at 37°C. Four days later, a partially acid-fast, branching gram-positive rod identified initially as *Nocardia* species was reported to be growing. On the 20th hospital day the patient became lethargic, pulmonary status deteriorated, and repeated chest radiography showed extensive bilateral lower lobe infiltrates. Based on microbiological findings, intravenous amikacin (500 mg three times a day) and trimethoprim/sulfamethoxazole (15 mg/kg of body weight/day) was initiated. The patient died on day 22 of hospitalization.

The isolate was resistant to lysozyme (50 μg/ml) and was initially identified as a member of the *N. asteroides* complex on the basis of its nondegradation of casein, tyrosine, xanthine, and hypoxanthine. The isolate was identified as *N. farcinica* on the basis of equal growth at 35 and 45°C; opacification of Middlebrook 7H10 agar; lack of arylsulfatase (2-week test); and resistance to gentamicin, tobramycin, erythromycin, and cefotaxime (3). Susceptibility testing was performed by broth microdilution (Dade MicroScan Inc., West Sacramento, Calif.) and the disk diffusion test on Mueller-Hinton agar; the mixture was incubated for 72 h at 35°C and interpreted according to NCCLS criteria for organisms that grow aerobically (8). The isolate was susceptible to imipenem (≤1 μg/ml), amikacin (≤8 μg/ml), ciprofloxacin (≤0.12 μg/ml), trimethoprim/sulfamethoxazole (≤2/38 μg/ml), and tetracycline (≤4 μg/ml) and was resistant to ampicillin (>8 μg/ml), cefotaxime (>32 μg/ml), gentamicin (>8 μg/ml), tobramycin (>8 μg/ml), and erythromycin (>16 μg/ml).

Nocardia spp. grow slowly and can be easily overgrown by more rapidly proliferating bacteria, so a selective medium is essential for reliable isolation from contaminated specimens. Thayer-Martin and selective BCYE media are commonly used in clinical laboratories and are suitable for recovery of *Nocardia* spp. from nonsterile specimens such as sputa. BCYE for-

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mulation containing vancomycin rather than cefamandole may be more appropriate since the later antibiotic may inhibit some strains (5, 7). In our patient, *N. farcinica* was recovered from both media after 4 days of incubation.

In clinical laboratories, identification of *Nocardia* species is done on the basis of colonial and microscopic morphologies and growth in lysozyme and Gordon tests (6). Unfortunately, this scheme is unable to separate the species which comprise the *N. asteroides* complex. Wallace et al. have reported growth at 45°C, utilization of acetamide, acid production from rhamnose, and resistance to tobramycin and cefamandole as useful tests in the identification of *N. farcinica* (12). However, none of these tests are 100% sensitive or 100% specific. Moreover, some of them require materials not commonly available in clinical laboratories. A combination of growth at 45°C, opacification of Middlebrook 7H10 agar, and resistance to cefotaxime, tobramycin, and erythromycin provide a consistent discrimination (100%) between isolates of *N. asteroides* complex strains, and these tests are easy to perform and widely available in routine microbiology laboratories (3). Although methods of susceptibility testing for nocardiae have not yet been standardized, broth dilution and disk diffusion tests can provide useful information.

The incidence of nocardial infections in human and animal populations is not known; several reports indicate that such infections are underdiagnosed and that the incidence of infection is apparently increasing. It has been estimated that between 500 and 1,000 infections with *Nocardia* species occur yearly in the United States and between 150 and 250 in France (1, 2). Because of its controversial status, *N. farcinica* was not mentioned in the literature for some years, so the relative frequencies of *N. farcinica* among clinical nocardial isolates are difficult to determine and may vary geographically (2, 4, 9, 12).

Pulmonary disease in a patient with underlying immunosuppression is the most common presentation of *N. farcinica* infection. In a recent retrospective review of 53 cases of *N. farcinica* infections, 85% of the patients had predisposing factors (10). Chronic pulmonary disease was the underlying condition in five cases, and only one patient had not received steroid therapy. The case reported here had some unusual features: the patient had previously been mostly healthy except for a well-tolerated mild pneumoconiosis and never received steroid treatment.

Because of its low incidence, nocardiosis is usually not considered in the initial diagnosis and selective media are not routinely used. Identification by standard methods is a lengthy process that can delay the start of appropriate antibiotic therapy, and such a delay can have serious consequences. In the case reported here, the patient received cefotaxime and piperacillin/tazobactam but extensive pulmonary lesions developed and the patient died.

In conclusion, we advocate a high index of suspicion for nocardiosis even in previously healthy patients with pneumonia unresponsive to empirical broad-spectrum therapy and an active approach in obtaining optimal specimens for diagnostic studies. Selective media should be used, and if a *Nocardia* species is isolated, routine microbiology laboratories should attempt to identify it to species level and in vitro sensitivity tests should be performed.

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