Severe pneumonia due to *Nocardia otitidiscaviarum* identified by mass spectroscopy in a cotton farmer

**A case report and literature review**

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**Abstract**

**Rationale:** *Nocardia* species are aerobic saprophytic bacilli. Among *Nocardia* species, *Nocardia otitidiscaviarum* (N. otitidiscaviarum) is rarely reported in pulmonary infection.

**Patient concerns:** We reported a case of *N. otitidiscaviarum* pneumonia in a cotton farmer.

**Diagnoses:** *N. otitidiscaviarum* pneumonia was identified by mass spectroscopy.

**Interventions:** Combined treatments (amikacin, imipenem and trimethoprim-sulfamethoxazole) were administered after identification of *N. otitidiscaviarum*.

**Outcomes:** The patient eventually died from severe respiratory insufficiency in the hospital.

**Lessons:** Early precise diagnosis and prompt combined therapy are of vital importance in severe *Nocardia* pulmonary infection.

**Keywords:** mass spectroscopy, *Nocardia otitidiscaviarum*, severe pneumonia

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1. Introduction

*Nocardia* species consist of gram-positive, variably acid-fast, strictly aerobic Saprophytic, and rod-shaped bacteria, which show branching filamentous forms and are ubiquitous in the environment, particularly in soil rich in organic matter, decaying vegetation, and standing water.[¹,²] Out of all *Nocardia* species, *Nocardia asteroides*, *Nocardia farcinica*, and *Nocardia brasiliensis* are the primarily pathogens causing nocardiosis, while other species are rarely or infrequently reported.[³–⁶] As one of the less commonly isolated *Nocardia* species,[⁷] *N. otitidiscaviarum* is considered to be less pathogenic than other species of *Nocardia*.[⁸,⁹] Herein we present a case of *N. otitidiscaviarum* pulmonary infection.

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2. Case report

A 58-year-old cotton farmer was presented to the West China Hospital of Sichuan University because of an over 1-month history of recurrent fever (between 38 and 40°C), productive cough, and dyspnea. Prior to admission, he was diagnosed of pneumonia and treated with latamoxef, ofloxacin, vancomycin, and voriconazole at local hospital. However, no remission of symptoms was observed. Moreover, he was a hepatitis B virus carrier with a 10 pack-years smoking history. However, no history of diabetes mellitus, tuberculosis, and use of glucocorticoids in the past were informed.

On admission, blood pressure, 145/95 mmHg; heart rate, 120 per minute; respiratory rate, 30 per minute; and temperature, 39.3°C. Physical examination revealed diminished breath sounds, but no rales were heard, and evaluation of other systems was unremarkable except moderate edema of lower limbs. Arterial blood gases analysis showed pH 7.361, PCO₂ 53.5 mm Hg, and PO₂ 62.8 mmHg. Laboratory data (Table 1) revealed leukocytosis of 49,500/mm³ with 97.4% neutrophils, and elevated procalcitonin of 5.16 ng/mL. Chest computed tomography, presence of nodules, masses, patchy consolidations, and bilateral pleural effusion, is noted (Fig. 1A). Meanwhile, it was soon alerted in sputum smear with presence of filamentous, gram-positive, weakly acid-fast, and beaded bacilli with possible diagnosis of *Nocardia* infection (Fig. 1B, C). Trimethoprim-sulfamethoxazole (3 pills per 6 hours) with noninvasive ventilation was promptly administered. Sputum culture showed growth of numerous bacteria that were precisely determined to be *N. otitidiscaviarum* by the method of mass spectroscopy on day 6 after admission (Fig. 1D). Antibiotics were thus modified to amikacin and imipenem in addition to trimethoprim-sulfamethoxazole in accordance with the sensitivity test. However, the patient was not improved as expected and eventually died from severe respiratory insufficiency on the 13th hospital day.

This case report was approved by the Institutional Review Board of West China Hospital of Sichuan University, and the informed consent was obtained.
3. Discussion

*Notitidiscaviarum*, formerly called *Nocardia caviae*, was first obtained from the middle ear of an infected Sumatran guinea pig and reported by Snijders in 1924,\[10\] while 1st report of cases of human infection by *Notitidiscaviarum* did not reach the literature until the mid-1960s.\[11\] In spite of the fact that nocardiosis are being increasingly recognized, infections due to *Notitidiscaviarum*, comprising about only 0.3% to 2.9% of all *Nocardia* infections,\[12\] remain infrequently reported.\[13\] Beaman et al described that only 10 cases from 347 patients infected by *Nocardia* in United States were identified as *N. otitidiscaviarum* infection.\[14\] Similarly, Kageyama et al\[14\] reported that out of more than 303 pathogenic *Nocardia* strains isolated from nocardiosis patients in Japan from 1992 to 2001, only 14 were identified as *N. otitidiscaviarum*. This low incidence of *N. otitidiscaviarum* may be attributed to its lower prevalence in the environment when compared with other *Nocardia* species,\[15,16\] although it has been found to be native to the soil.\[17\] In this case, the cotton farmer had intimate contact with the soil, which increased the risk for *N. otitidiscaviarum* infection.

Noticeably, *N. otitidiscaviarum* has been described as an opportunistic pathogen in human.\[7\] However, it has been reported in both immunocompromised and immunocompetent individuals to be a cause of pulmonary, primary cutaneous, and lymphocutaneous infections.\[12\] Individuals with weakened immune system, such as patients suffering from diabetes mellitus, chronic obstructive pulmonary disease, mixed connective tissue disorder, ulcerative colitis, cirrhosis, human immunodeficiency virus infection, malignancies, those receiving long-term or large dose of corticosteroid therapy, and bone marrow or solid organ transplant, are at higher risk.\[18–20\] In this case, the patient has no immunocompromised disorders, but 10 pack-years smoking history, which could be a risk factor to weaken the defense capability in lungs.

Being relatively rarely reported, *N. otitidiscaviarum* is postulated to be less pathogenic in human when compared with other *Nocardia* species.\[8,9\] However, contradictory results have been yielded from animal studies of nocardial virulence.\[10\] Smith and Hayward\[21\] reported that *N. otitidiscaviarum* and *N. asteroides* were of similar virulence; Mishra et al\[22\] confirmed that the 2 species were of equal pathogenicity and were both markedly more virulent than *N. brasiliensis*. It is likely that the pathogenicity of *N. otitidiscaviarum* varies due to different strain.

**Table 1**

| Results of laboratory tests during 13 days of disease course. | Day 1 | Day 7 | Day 13 |
|------------------------------------------------------------|-------|-------|--------|
| WBC, 10⁹/L                                                | 49.5  | 15.3  | 16.2   |
| N%                                                        | 97.4  | 91.4  | 91.5   |
| TBIL, μmol/L                                              | 6.1   | 6.7   | 4.6    |
| ALT, IU/L                                                 | 17    | 11    | 11     |
| TP, g/L                                                   | 48.2  | 45.2  | 43.4   |
| ALB, g/L                                                  | 21.3  | 21.1  | 17.3   |
| PCT, ng/mL                                                | 5.16  | 2.28  | 3.21   |
| CRP, mg/L                                                 | 236   | 141   | 156    |
| Pre-BNP, pg/mL                                             | 1066  | –     | 1471   |
| FDP, pg/mL                                                | 19.3  | –     | 36.6   |
| CRP-test, pg/mL                                           | –     | –     | –      |
| GM-test (OD)                                               | 0.03  | –     | –      |
| HBV-DNA, copies/mL                                        | –     | –     | –      |
| CMV-DNA, copies/mL                                        | –     | –     | –      |
| EBV-DNA, copies/mL                                        | –     | –     | –      |
| HIV-DNA, copies/mL                                        | –     | –     | –      |
| TB-DNA, copies/mL                                         | –     | –     | –      |
| Mp-IgM                                                    | –     | –     | –      |

Alb = albumin, ALT = alanine transaminase, BNP = brain natriuretic peptide, CMV = cytomegalovirus, CRP = C-reactive protein, DNA = deoxyribonucleic acid, EBV = Epstein-Barr virus, FDP = fibrin degradation products, HBV = hepatitis B virus, HIV = human immunodeficiency virus, Ig = immunoglobulin, Mp = mycoplasma, N = neutrophil, OD = optical density, PCT = procalcitonin, TB = tuberculosis, TBIL = total bilirubin, TP = total protein, WBC = white blood cell.

**Figure 1.** (A) Chest computed tomography (CT) image, (B) gram-positive staining, (C) weakly acid-fast staining, and (D) mass spectroscopy graph for *Nocardia otitidiscaviarum*. 
variability, inoculum size, and infection route. Moreover, human infections by *N. otitidiscaviarum* usually occur in 2 major forms, the pulmonary form (through direct inhalation of pathogen or bacteria fragments carried in dust or spores) and the cutaneous form (following injection by a thorn prick or similar accidents). There has not been any case report of human-to-human or animal-to-human transmission. Obviously, this case prefers the pulmonary form.

With signs, symptoms, and imaging features being not pathognomonic, it is challenging to clinically diagnose *N. otitidiscaviarum* infection. Conventional evaluation of specimens like sputum samples, abscesses, wound drainages, or bronchial washings by smear and culture remains the principal method of diagnosis. Yet, it is noteworthy that almost 1 week or even more may be needed for the presence of *N. otitidiscaviarum* to be noted on cultures on routine bacteriologic media because of its slow growth. However, relative to the conventional methods, polymerase chain reaction and 16S rDNA sequencing, or mass spectroscopy used in this case are much more rapid precise, and accurate in identifying *N. otitidiscaviarum*. *N. otitidiscaviarum* infection calls for long-course drug treatment, and it is suggested that antibiotic therapy should be continued for 6 months in immune competent patients and up to a year in immunosuppressed patients. Although increasing numbers of *Nocardia* species including *N. otitidiscaviarum* complex have developed increasing resistance and demonstrated inconsistent susceptibility to trimethoprim-sulfamethoxazole, sulfonamides developed increasing resistance and demonstrated inconsistent susceptibility to trimethoprim-sulfamethoxazole, sulfonamides remain the standard antimicrobial agents for the treatment of nocardiosis to date. Most *N. otitidiscaviarum* isolates are also reported to be resistant to and beta-lactams like ampicillin, amoxicillin-clavulanic acid, and imipenem, but are usually susceptible to amikacin and the fluoroquinolones. Meanwhile, some other studies have shown that *N. otitidiscaviarum* complex is proved to be sensitive to linezolid in vitro; however, data from in vivo studies are lacking. In addition, incidence of hematologic toxicity becomes higher after 4 weeks of linezolid application, and clinical experience with linezolid is limited. Antimicrobial susceptibility testing can guide the treatment of *N. otitidiscaviarum*, and the US National Committee for Clinical Laboratory Standards approved an antimicrobial testing of aerobic actinomycetes including *Nocardia* by using broth microdilution. Although the optimal treatment protocol of *N. otitidiscaviarum* still unknown, a combination of sulfonamides and amikacin with a carbapenem or a 3rd-generation cephalosporin are suggested still unknown, a combination of sulfonamides and amikacin with a carbapenem or a 3rd-generation cephalosporin are suggested.

In conclusion, *N. otitidiscaviarum* infection is rarely reported and requires early diagnosis and prompt intervention. Considering the high rate of mortality, long-course treatment with optimal protocol is desperately needed.

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References

[1] Kandi V, Human Nocardia infections: a review of pulmonary nocardiosis. Cureus 2015;7:e304–1304.
[2] Lerner PI. Nocardiosis. Clin Infect Dis 1996;22:891–903.
[3] Szabolle MA, Sussland D. Nocardiosis: review of clinical and laboratory experience. J Clin Microbiol 2003;41:4497–501.
[4] Beaman BL, Burnsje J, Edwards B, et al. Nocardial infections in the United States, 1972–1974. J Infect Dis 1976;134:286–9.
[5] Boiron P, Provost F, Chevrier G, et al. Review of nocardial infections in France 1987 to 1990. Eur J Clin Microbiol Infect Dis 1992;11:709–14.
[6] Menendez R, Cordero PJ, Santos M, et al. Pulmonary infection with *Nocardia* species: a report of 10 cases and review. Eur Respir J 1997;10:1542–6.
[7] Brown-Elliot BA, Brown JM, Connville PS, et al. Clinical and laboratory features of the *Nocardia* spp. based on current molecular taxonomy. Clin Microbiol Rev 2006;19:239–82.
[8] Schlaberg R, Huard RC, Della-Latta P. Nocardia cyrissaegeorgica, an emerging pathogen in the United States. J Clin Microbiol 2008;46:263–73.
[9] Castelli L, Zlotnik H, Ponti R, et al. First reported *Nocardia otitidiscaviarum* infection in an AIDS patient in Italy. Mycopathologia 1994;126:131–6.
[10] Clark NM, Braun DK, Pastorak A, et al. Primary cutaneous *Nocardia otitidiscaviarum* infection: case report and review. Clin Infect Dis 1995;20:1266–70.
[11] Hemmersbachmiller M, Martel AG, Benitez AB, et al. Brain abscess due to *Nocardia otitidiscaviarum*: report of a case and review. Scand J Infect Dis 2004;36:381–4.
[12] Ishihara M, Takada D, Sugimoto K, et al. Isolation of *Nocardia otitidiscaviarum* from sputum of a patient with bronchiectasis. Jpn J Med Microbiol 1984;28:193–8.
[13] Corri ME, Villafane-Fioti MF. Nocardiosis: a review. Intern J Infect Dis 2004;8:321–7.
[14] Shahapur PR, Peerapur BV, Shahapur RP, et al. Lymphocutaneous nocardiosis caused by *Nocardia otitidiscaviarum*: a case report and review of literature. J Nat Sci Biol Med 2014;5:197–201.
[15] Kagesyama A, Yazaka K, Ishikawa J, et al. Nocardial infections in Japan from 1992 to 2001, including the first report of infection by *Nocardia transvalensis*. Eur J Epidemiol 2004;19:383–9.
[16] Ramamoorthi K, Pruthvi BC, Rao NR, et al. Pulmonary nocardiosis due to *Nocardia otitidiscaviarum* in an immunocompetent host – a rare case report. Asian Pac J Trop Med 2011;4:414–6.
[17] Kurup PV, Randhawa HS, Sandhu RS. A survey of *Nocardia asteroides*, *N. canina* and *N. brasiliensis* occurring in soil in India. Sabouraudia 1968;6:260–6.
[18] Causey WA. Nocardia caviae complex. J Clin Microbiol 2003;41:259.
[19] Khadiz M, Hosseini M, Mackinnon ACJr, et al. Disseminated nocardiosis with *N. asteroides* following injection by a thorn prick. Dermatol Surg 2012;15:163–70.
[20] Yildiz O, Doganay M. Actinomyces and *Nocardia* pulmonary infections. Curr Opin Pulm Med 2006;12:228–34.
[21] Smith IM, Hayward AH. Nocardia caviae and *Nocardia asteroides*: comparative bacteriological and mouse pathogenicity studies. J Comp Pathol 1971;81:79–87.
[22] Mishra SK, Sandhu RS, Randhawa HS, et al. Effect of cortisone administration on experimental nocardiosis. Infect Immun 1973;7:123–9.
[23] Kim J, Kang M, Kim J, et al. A case of *Nocardia farcinica* pneumonia and mediastinitis in an immunocompetent patient. Tuberc Respir Dis 2000;31:1209–15.
[24] Patel MCS, Varghese J, Rajagopalan N. A fatal case of pulmonary nocardiosis. BMJ Case Rep 2012doi: 10.1136/bcr.09.2011.4875.