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Pulmonary nocardiosis: A clinical analysis of 59 cases

Yu Kurahara[a], Kazunobu Tachibana[a,b], Kazunari Tsuyuguchi[b], Masanori Akira[c], Katsuhiro Suzuki[a,*], Seiji Hayashi[a]

[a]Department of Internal Medicine, National Hospital Organization Kinki-Chuo Chest Medical Center, Osaka, Japan
[b]Clinical Research Center, National Hospital Organization Kinki-Chuo Chest Medical Center, Osaka, Japan
[c]Department of Radiology, National Hospital Organization Kinki-Chuo Chest Medical Center, Osaka, Japan

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ABSTRACT

Background: Pulmonary nocardiosis is a rare but severe infection caused by *Nocardia* species. This study aimed at describing the clinical characteristics and prognosis of pulmonary nocardiosis.

Methods: An observational, retrospective study was undertaken of patients diagnosed with pulmonary nocardiosis over a 13-year period at the Kinki-Chuo Chest Medical Center, Osaka, Japan.

Results: Seven patients with airway nocardial colonization and 59 patients with pulmonary nocardiosis were identified, one of whom had disseminated nocardiosis. Patients with pulmonary nocardiosis were predominantly male patients (73%), with a mean age of 66 (range, 15–88) years. New-onset cough and dyspnea were the most common manifestations (76%). Although 52 (88%) patients had at least one underlying pulmonary disease, most patients did not appear to be systemically immunocompromised. The predominant abnormality on chest computed tomography in pulmonary nocardiosis was airspace consolidation (52%), sometimes associated with cavitation. Multivariate Cox proportional-hazards analysis revealed the following significant and independent risk factors for overall mortality: age >68 years (hazard ratio [HR], 4.7; 95% confidence interval [CI], 1.6–14; $p=0.05$), pulmonary aspergillosis (HR, 8.8; 95% CI, 2.4–33; $p=0.01$), and trimethoprim/sulfamethoxazole (TMP-SMZ) resistance (HR, 4.3; 95% CI, 1.6–11; $p=0.04$).

Conclusions: Clinicians should be aware that pulmonary nocardiosis can occur even in immunocompetent patients, especially those with an underlying pulmonary disease. In pulmonary nocardiosis, older age, pulmonary aspergillosis, and TMP-SMZ resistance are associated with increased risk of mortality.

Abbreviations: CI, confidence interval; CT, computed tomography; HR, hazard ratio; TMP-SMZ, trimethoprim/sulfamethoxazole

*Corresponding author. Tel.: +81 72 252 3021; fax: +81 72 251 1372.
E-mail addresses: yukurahara@kch.hosp.go.jp (Y. Kurahara), ktachiba@kch.hosp.go.jp (K. Tachibana), tsuyuguchi@kch.hosp.go.jp (K. Tsuyuguchi), akira@kch.hosp.go.jp (M. Akira), ksuzuki@kch.hosp.go.jp, krawelts@yahoo.co.jp (K. Suzuki), shayashi@kch.hosp.go.jp (S. Hayashi).

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1. Introduction

The *Nocardia* genus of aerobic gram-positive bacteria causes a range of infectious diseases, including isolated pulmonary and skin infections and disseminated disease [1]. Pulmonary nocardiosis is a rare but severe infection that commonly presents as a subacute or chronic disease, mimicking lung cancer or other pulmonary infections such as mycosis or bacterial pneumonia. There are more than 90 *Nocardia* species, at least 33 of which cause disease in humans [2].

Because of changes in taxonomy and the difficulty inherent in the routine identification of *Nocardia* strains at the species level, there have been few published studies concerning pulmonary nocardiosis [3–8]. Of those that have been conducted, most have investigated only patients with immunosuppression and have included only a small number of patients. Moreover, the details of the clinical characteristics and prognosis of pulmonary nocardiosis remain unclear. The objective of the present study is to clarify the characteristics of pulmonary nocardial patients and to elucidate the factors that determine its etiology and prognosis.

2. Materials and methods

2.1. Study Subjects

We aimed at studying the clinical pattern of pulmonary nocardiosis in the Kinki-Chuo Chest Medical Center, Osaka, Japan, based on a retrospective review of cases from January 1999 to October 2012. The hospital is a 450-bed respiratory disease center designed to manage patients with various respiratory diseases. In the present study, patients with no evidence of pulmonary disease or symptoms of respiratory infection despite the isolation of *Nocardia* species were defined as having airway nocardial colonization. Pulmonary nocardiosis was defined as the presence of symptoms of respiratory infection consistent with pulmonary nocardiosis, with *Nocardia* species isolated from respiratory sample cultures on at least one occasion. Disseminated nocardiosis was defined as an infection in two noncontiguous organs or in the central nervous system. This study was approved by the Institutional Review Board at the Kinki-Chuo Chest Medical Center (Approval date: November 14, 2011; Approval number: 388).

2.2. Microbiological identification

In order to diagnose pulmonary nocardiosis, samples were examined microscopically after Gram staining in order to determine the presence of microorganisms and establish specimen quality. The presumptive identification of *Nocardia* species was based on the microscopic characteristics of the isolates and the macroscopic morphology of the colonies. Although 16S ribosomal RNA sequence-based identification of *Nocardia* species has recently become the gold standard, this technology was not available in our laboratories during the study period. Therefore, *Nocardia* isolates were identified using a combination of traditional standard biochemical tests, growth characteristics, and antimicrobial susceptibility patterns. Hence, the microbiological notation was rendered in its traditional form in this study. The susceptibility of the isolates was determined by the disc diffusion method. A total of 90 specimens from 66 patients were identified as culture-proven *Nocardia*.

2.3. Radiographic assessment

Three pulmonary infectious disease experts (Y.K., K. Tachibana., and K.S.) and one chest radiologist (M.A.) retrospectively reviewed de-identified computed tomography (CT) films. The reviewers classified each case based on the presence of the following features: (1) airspace consolidation; (2) nodules (defined as those with diameters <3 cm); (3) cavity; (4) consolidation with cavity; (5) pleural effusion; and (6) indeterminate (we anticipated the possibility that some cases had an underlying pulmonary condition indistinguishable from pulmonary nocardiosis because of the complicated structure of lung fields). Any inconsistencies were resolved by consensus.

2.4. Study variables

The following data were collected: patient demographics, comorbidities, immunological state, clinical manifestations, radiographic findings, bacteriological reports, susceptibility to trimethoprim/sulfamethoxazole (TMP-SMZ), treatment course, and survival time from diagnosis.

2.5. Statistical analysis

Statistical analysis was performed with SPSS version 15.0J software (SPSS Inc., Chicago, Illinois), and the Kaplan–Meier method was used for survival analysis. If the patient died or was lost to follow-up during the study period, this was recorded as censored data. A univariate assessment of selected risk factors was performed using a Cox proportional hazard model. To eliminate confounding factors in predicting mortality risk, variables with P values <0.05 on univariate analysis were then entered into a multivariate assessment. We used a Cox proportional hazard model with a step-up procedure, utilizing the likelihood ratio as the criterion for adding significant variables. Results are expressed as hazard ratios with corresponding 95% confidence intervals (CI). A P value of <0.05 was regarded as significant.

3. Results

3.1. Characteristics and clinical features of the patients

A total of 90 respiratory specimens from 66 patients were identified as culture-proven *Nocardia*. Seven patients were diagnosed with airway nocardial colonization because they had minimal or no lung-field lesions and the absence of respiratory symptoms. These lesions remained stable after at least 1 year of follow-up, during which time no treatment was given. In total, 59 patients were diagnosed with pulmonary nocardiosis (43 male patients and 16 female patients). One