

High-resolution CT findings of patients with pulmonary nocardiosis

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ABSTRACT

Background: Opportunistic pulmonary infection with *Nocardia* species is rare in humans, and only a few studies have radiologically analyzed patients with pulmonary nocardiosis using high-resolution computed tomography (HRCT).

Methods: We retrospectively reviewed the medical records of patients with pulmonary nocardiosis at our hospital between April 2006 and December 2011 to assess HRCT and clinical findings. We also searched the medical literature for pulmonary nocardiosis reported in Japan between 2002 and 2011 for comparison.

Results: We identified seven patients at our institution and 33 reported infections in Japan. Four of our patients were immunocompetent, whereas the other three had impaired cellular immunity due to type 2 diabetes mellitus or having been inappropriately treated with steroid. Thoracic HRCT revealed no zonal predominance, but tropism for distribution from the middle to the peripheral area, and radiological findings of nodules, cavitation, mass, consolidations, bronchial wall thickening, septal line thickening and ground glass opacity (GGO) were evident. The main HRCT finding in our study comprised nodules (n=5, 71.4%) <30 mm and four patients had multiple nodules as described in other reports. Furthermore, we discovered a crazy paving appearance (CPA) around nodules, cavities, masses or consolidations in five patients (71.4%).

Conclusions: Multiple nodules distributed from the middle to the peripheral area on HRCT might reflect pulmonary nocardiosis, and CPA seemed to be a worth paying attention to the diagnosis.

KEY WORDS

Crazy paving appearance; multiple nodules; lung infections; opportunistic pathogen; pulmonary nocardiosis

J Thorac Dis 2012;4(6):577-582. DOI: 10.3978/j.issn.2072-1439.2012.11.07

Introduction

Nocardia is a rare opportunistic pathogen that particularly affects immunocompromised patients, and only a few reports have described high resolution computed tomography (HRCT) manifestations in a case series of pulmonary infection (1-7). Although HRCT plays an important role in the diagnosis of pulmonary nocardiosis, variations in HRCT findings have not correlated with clinical diagnosis. Here, we describe the

radiological features of pulmonary nocardiosis with respect to pulmonary nodules. Impaired cell-mediated immunity would increase the prevalence of infection (8-10), however, there was no study to examine the status of cumulative and/or daily dose of steroid treatment in patients with pulmonary nocardiosis. The aim of this study is to assess the HRCT findings in pulmonary nocardiosis reported in Japan together with examine the effects of steroid treatment in individual patients.

Methods

Data sources

We conducted a retrospective review of the medical records at our hospital between April 2006 and December 2011 and identified 16 consecutive patients with pulmonary nocardiosis. We analyzed the clinical and radiological findings of these patients. The inclusion criteria were the presence of *Nocardia* spp. in sputum or bronchoscopic samples from the respiratory

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Submitted Oct 04, 2012. Accepted for publication Nov 14, 2012.
Available at www.jthoracdis.com

ISSN: 2072-1439

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Table 1. Clinical demographics of patients (n=7).

Patient No.	Species	Sex	Age	Current use of steroid/cumulative dose	Diagnostic method	Prognosis
1	<i>Nocardia farcinica</i>	F	78	-/-	Sputum	Alive
2	<i>Nocardia abscessus</i>	F	77	-/-	Sputum	N.A.
3	<i>Nocardia farcinica</i>	M	74	15 (mg/day)/8,270 (mg)	Sputum	Alive
4	<i>Nocardia</i> sp.	F	84	-/3,000 mg	Sputum	Dead
5	<i>Nocardia</i> sp.	M	51	-/-	Bronchoscopy	Alive
6	<i>Nocardia</i> sp.	F	43	-/-	Sputum	Alive
7	<i>Nocardia asisttica</i>	M	66	35(mg/day)/7,314 (mg)	Bronchoscopy	Alive

tract. Nine of the 16 patients were excluded from this study because CT images were missing, leaving a total of 7 patients (male:female, 3:4; average (mean \pm S.D) age at the diagnosis, 67.6 \pm 15.2 years). The species of four *Nocardia* strains isolated from the seven patients were determined by 16S ribosomal DNA sequencing (11). We also searched the medical literature to find reports of pulmonary nocardiosis in Japan between 2002 and 2011 to compare our findings. We identified 33 patients (average (mean \pm S.D). age at diagnosis, 59.2 \pm 15.2 y; male:female, 2:1) who were evaluated by HRCT. Pulmonary radiologists with >15 years of experience who were blinded to the clinical findings of the patients independently reviewed the images, and decisions images were interpreted by consensus. The definition of the interpretations followed the Glossary of Terms for Thoracic Imaging proposed by the Fleischner Society (11). We then evaluated correlations between radiological and clinical findings in our patients, and compared the radiological findings with those of published reports. This retrospective study was approved by the Ethical Board of Kyorin University (Mitaka, Tokyo, Japan).

Statistical analysis

Data were statistically analyzed using Pearson's chi-square test or the Mann-Whitney test and SPSS version 19. A P value of <0.05 in paired two-sided tests was judged to represent statistical significance.

Results

Clinical features of our and reported patients

Table 1 shows the clinical demographics of our seven patients and Table 2 (12-30) summarizes the clinical findings in these and published reports of 33 patients Japan (Table 2) (31-43). The following *Nocardia* strains were identified in four of our patients: *N. farcinica* (Patients 1 and 3); *N. abscessus* (Patient 2); and *N. asiatica* (Patient 7). Those in the published cases were *N. asteroides* (n=8, 24.2%) and *N. farcinica* (n=8, 24.2%), followed

by *N. otitidiscaviarum* (n=3, 9.0%) (Table 3). Underlying disease affected 57.1% (n=4) of our patients and 72.7% (n=24) of reported patients (Table 2). Two of our patients (Patients 3 and 4; 28.6%), were treated with steroid, one (Patient 7; 14.3%) was treated with steroid plus an immunosuppressive drug, and four (Patients 1, 2, 5, and 6; 57.1%) were not treated compared with 10 (30.3%) 7 (21.2%), and 15 (45.5%) previously reported cases, respectively. The total cumulative dose administered to our three patients with a history of steroid therapy ranged from 3,000 to 8,270 mg and two patients had used steroids within 1 year (Patients 3 and 7; 15 and 35 mg/day, respectively; Table 1). The clinical manifestations in our and reported patients were, respectively, productive cough (n=6, 85.7%; n=10, 30.3%), pyrexia (n=6, 85.7%; n=12, 36.4%), sputum (n=0, 0%; n=4, 12.1%), and dyspnea (n=3, 42.9%; n=3, 9%). Seven (21.2%) reported patients had abscesses, whereas ours had none (Table 2).

Radiological findings

Thoracic HRCT showed no zonal predominance in our case series, but predominant distribution from the middle to the peripheral area (Table 4). Figure 1 shows the major representative HRCT findings in our patients (Figure 1). Although various radiological findings such as cavitations, masses, consolidations, bronchial wall and septal line thickening, as well as ground glass opacity, were evident in the present and previous patients (1-5), the main findings in the present study comprised nodules (n=5, 71.4%). Four patients had multiple nodules. We could not obtain detailed HRCT findings with respect to the size and distribution from the reported cases (Table 5), but cavitations were the most prevalent (33.3%), followed by nodules (24.2%). Seven among the 33 reported patients had multiple nodules and one had a solitary nodule, which was a similar trend as the present study. Of note, crazy paving appearance on HRCT were commonly observed in our five cases (71.4%), but statistical significance between the groups with or without CPA was not detected regarding with their clinical findings such as the severity of fever and serum inflammatory markers.

Table 2. Patients' characteristics and presenting symptoms.

	Our patients	Previously reported cases
Total number of patients	7	33
age \pm SD	67.6 \pm 15.2	59.2 \pm 15.2
M:F	3:4	22:11
Underlying disease -	3	9
Underlying disease +	4	24
Metabolic & Endocrine		
NIDDM type2	1	5
Cushing disease	0	1
CVD		
SLE	0	2
MPA	0	2
Lung disease		
IIPs	2	2
HP	0	1
BE	0	2
DPB	1	0
Renal disease		
Post transplantation	0	3
Membranous nephropathy	0	3
Nephrotic syndrome	0	1
Lupus nephritis	0	2
Malignancy		
Malignant lymphoma	2	1
Cardiac disease		
CHF	1	1
AV block (III)	1	0
HOCM	1	0
Miscellaneous		
AIHA	0	1
Drug		
Steroid only	2	10
Steroid + immunosuppressive drug	1	7
Immunosuppressive drug only	0	1
None	4	15
Symptom		
Productive cough	6	10
Pyrexia	6	12
Sputum	0	4
Dyspnea	3	3
Disturbance of consciousness	0	1
Abscess	0	7
General malaise	0	3
Hemoptysis	0	1
Chest pain	0	1
Headache	0	1

Table 3. Nocardia species in our and other patients.

Species	Our patient (n=7)	Published reports (n=33)
<i>N. sp.</i>	3	8
<i>N. asteroides</i>	0	8
<i>N. farcinica</i>	2	8
<i>N. otitidiscaviarum</i>	0	3
<i>N. nova</i>	0	2
<i>N. beijingensis</i>	0	1
<i>N. cyriacigeorgica</i>	0	1
<i>N. brasiliensis</i>	0	1
<i>N. farcinica</i> + <i>N. cyriacigeorgica</i>	0	1
<i>N. asiatica</i>	1	0
<i>N. abscessus</i>	1	0

Table 4. Radiological findings from 7 patients in the present study.

Number of patients (n)	7
Distribution	
Zonal predominance	
Upper	2 (28.6%)
Middle	1 (14.3%)
Lower	2 (28.6%)
Random	2 (28.6%)
Anatomical predominance	
Central	0
Middle	4 (57.1%)
Peripheral	3 (42.9%)
Random	0
Main radiological findings	
Nodule (<3 cm)	5 (71.4%)
Cavitation	1 (14.3%)
Mass (\geq 3 cm)	0
Consolidation	1 (14.3%)
Other radiological findings	
Bronchial ectasis	4 (57.1%)
Bronchial wall thickening	5 (71.4%)
Septal line thickening	6 (85.7%)
Centrilobular nodule	1 (14.3%)
Ground glass opacity	6 (85.7%)
Crazy paving like pattern	5 (71.4%)
Pleural effusion	4 (57.1%)

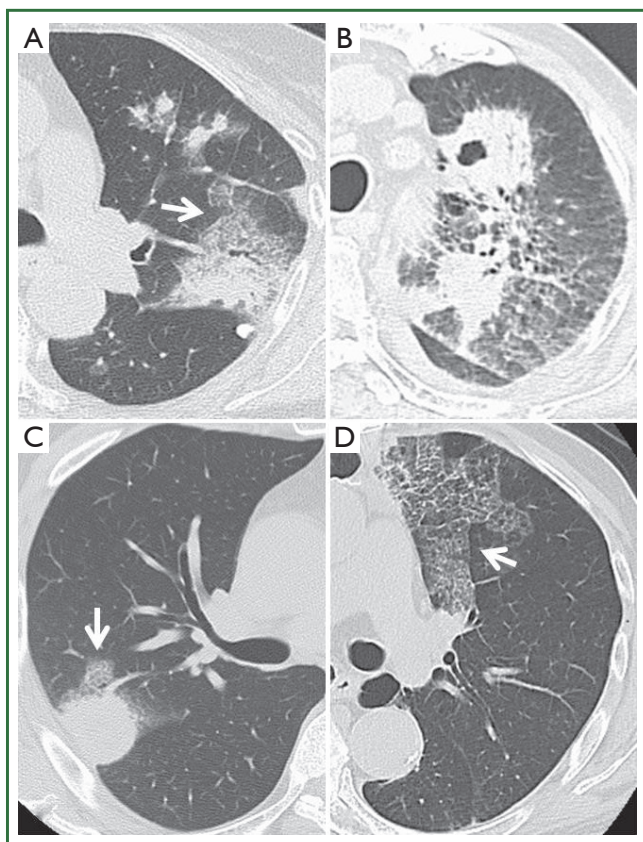


Figure 1. Representative HRCT findings of our patients at diagnosis. A. Air-bronchogram shows consolidation surrounded by CPA (arrow) and scattered nodules with GGO in Patient 1; B. Solitary nodule and cavity measure 27 and 28 mm, respectively, in Patient 3; C. Solitary 28-mm nodule surrounded by CPA (arrow) in Patient 5; D. Septal line thickening with CPA (arrow) in Patient 7.

Discussion

Various HRCT findings of pulmonary nocardiosis have been reported such as nodules/masses, consolidation/infiltrates, pleural thickening, and cavities (2-4,44). Furthermore, ground glass opacity with superimposed septal thickening and intralobular reticulation was found (45,46), which initially thought to be specific alveolar proteinosis. The total area of lung inflammation on HRCT images and/or the elevation of serum inflammatory markers in the present study seemed irrelevant to the presence of CPA. To the best of our knowledge, HRCT findings of CPA have not been described, which might have been underestimated in pulmonary nocardiosis. Blackmon *et al.* (4) reported that 57% cases revealed discrete nodules with a tendency for multiple in number, which were also predominant findings in previous reports and in our case series. Oszoyoglu *et al.* (3) also reported that the most commonly described findings were nodules and cavities. The main HRCT findings in the present study were lung nodules, which tended to be multiple without a

Table 5. Main radiological findings of our and other patients.

	Our patients (n=7)	Published reports (n=33)
Nodule (<3 cm)	5 (71.4%)	8 (24.2%)
Solitary	1	1
Multiple	4	7
Cavitation	1 (14.3%)	11 (33.3%)
Solitary	0	3
Multiple	1	8
Mass (≥3 cm)	0	5 (15.1%)
Solitary	0	4
Multiple	0	1
Consolidation	1 (14.3%)	8 (24.2%)
Empyema	0	1 (0.03%)

zonal preponderance, but were predominantly distributed in the middle to the peripheral area.

Stuck *et al.* (9) found 12.7% and 8.0% overall rates of infectious complications in steroid-treated and control patients, respectively (relative risk: 1.6), and Klein *et al.* (8) reported that the rate of infection did not increase in patients administered with <10 mg/day or a cumulative dose of <700 mg of prednisone. Indeed, three of our patients were administered >15 mg/day or a cumulative dose of 3,000 mg of prednisone. The present study is the first to review and examine the effects of daily and cumulative steroid dosing in patients with pulmonary nocardiosis. We also reconfirmed that immunocompetent patients might be infected with *Nocardia*.

Conclusions

The HRCT findings of pulmonary nocardiosis were diverse and multiple nodules found from the middle to the peripheral area were diagnostic clues. Crazy paving appearance might be a noticeable HRCT findings previously have not been described. Greater understanding and recognition of these findings might result in more rapid and appropriate diagnoses of affected patients.

Acknowledgements

Disclosure: The authors declare no conflict of interest.

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Cite this article as: Tsujimoto N, Saraya T, Kikuchi K, Takata S, Kurihara Y, Hiraoka S, Makino H, Yonetani S, Araki K, Ishii H, Takizawa H, Goto H. High-resolution CT findings of patients with pulmonary nocardiosis. *J Thorac Dis* 2012;4(6):577-582. DOI: 10.3978/j.issn.2072-1439.2012.11.07