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ORIGINAL RESEARCH

Comparison of Clinical Characteristics and Treatment Outcome Between Localized and Disseminated Nocardiosis in a Tertiary Hospital in China

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Background: In China, due to the large population, infections caused by Nocardia may not be as rare. Unfortunately, there is still inadequate knowledge of the clinical impact caused by Nocardia. This study aimed to compare the clinical characteristics and treatment of localized and disseminated nocardiosis.

Methods: The clinical and microbiological data of patients diagnosed with nocardiosis in a tertiary hospital in Beijing from July 2011 to July 2021 were collected and retrospectively analyzed.

Results: Among the 54 nocardiosis cases, 34 cases were in the localized infection group, while 20 cases in the disseminated infection group. The proportion of patients with chronic structural lung disease was higher in the localized group (P=0.010). In contrast, patients with disseminated infections were more prone to receive long-term glucocorticoids and/or immunosuppressants (P=0.027). Pulmonary nodules were prominent features of imaging changes in patients with disseminated infections (P=0.027) whereas bronchial dilatation was more common in patients with localized infections (P=0.025). In addition, the disseminated group had longer average hospitalization days relative to the localized group (P=0.016), but there was no significant difference in mortality between them (P=0.942).

Conclusion: There were differences in the clinical profiles between patients with localized and disseminated nocardiosis in terms of clinical presentation, infection site, radiological features, treatment, and prognosis. These findings may provide references for the management and treatment of patients with nocardiosis.

Keywords: *Nocardia*, disseminated nocardiosis, immunosuppressive population

Introduction

Nocardia is a Gram-positive aerobic bacterium characterized by hyphae-like branching. It is a common pathogen in the environment, often found in soil, decomposing vegetation and other organic matter, as well as in fresh and salt water.[1] So far, more than 100 of species of *Nocardia* have been identified, among which over 40 species have been shown to be clinically relevant.[2] Notably, *Nocardia* is often regarded as an "opportunistic infection agent" and most infections usually occur in immunosuppressed individuals under chemotherapy, organ transplants or with immunodeficiency diseases. *Nocardia* was first reported in 1988, and it was reported that the annual incidence of Nocardia infection/colonization increased from 0.33 (1997–1998) to 0.87 (2007–2008) per 100,000 inhabitants in Quebec, Canada.[3] Pulmonary

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nocardiosis is the most common type of infection, and the main symptoms are fever, cough, shortness of breath, weight loss and night sweats. Additionally, extrapulmonary nocardiosis is also relatively common and can spread to the pleura, pericardium, mediastinum, and vena cava through hematogenous dissemination or continuous spread of necrotizing pneumonia. Disseminated nocardiosis may lead to the involvement of diverse systems, such as the central nervous system (CNS), soft tissue, blood, and lymph nodes.[4] The mortality rate for nocardiosis ranges from 7% to 44%, but is further increased in cases of disseminated bacteremia or cerebral abscesses.[5]

Based on the enormous heterogeneity of the genomes of diverse *Nocardia* species, their virulence and antibiotic susceptibility also vary.[6,7] Consequently, this may pose a serious challenge for treatment. It is worth noting that trimethoprim-sulfamethoxazole (TMP-SMX) appears to be a useful antibiotic for the control of *Nocardia* infections.[6] Unfortunately, resistance to TMP-SMX has already emerged. A multicenter survey in the USA retrospectively included 552 clinical Nocardia isolates and found that approximately 0.5% (3/552 isolates) of the strains were resistant to TMP-SMX.[8] Thus, based on the rare and aggressive nature of *Nocardia* infections, a comprehensive understanding of its clinical features, antibiotic drug susceptibility and therapeutic efficacy is desirable.

In China, due to the large population, infections caused by *Nocardia* may not be as rare. Unfortunately, there is still inadequate knowledge of the clinical impact caused by *Nocardia*. Currently, few studies have systematically examined the clinical features of localized and disseminated nocardiosis, despite the numerous variations that may exist in their clinical presentation and treatment. This may make it difficult for patients to benefit from current treatment regimens. Thus, we conducted a retrospective study to compare the clinical characteristics of patients diagnosed with localized and disseminated *Nocardia* infection in a tertiary hospital in Beijing.

Materials and Methods

Patients

In this study, we retrospectively analyzed the clinical characteristics, laboratory and imaging examinations, treatment and prognosis of patients diagnosed with nocardiosis at Peking Union Medical College Hospital from July 2011 to July 2021. The identification of *Nocardia* is based on the combination of matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) and traditional biochemical methods. The diagnosis of nocardiosis is based on the isolation and culture of *Nocardia* from suspected sites (bronchoalveolar lavage, blood, pleural fluid, cerebrospinal fluid, pus, conjunctival sac secretions, etc.) and/or tissue (lung biopsy, skin biopsy) on the premise of exclusion of contamination or colonization.[9]

Clinical Data Collection

Patients' demographics and medical records were retrieved using the Hospital Information System (HIS) and the Laboratory Information System (LIS). Specifically, clinical, imaging, and microbiological data were collected among the 54 patients including risk factors, clinical characteristics, laboratory tests, imaging features, microbiological findings, treatment regimens, and outcomes.

Definition of Localized and Disseminated Nocardiosis

The definitions of localized and disseminated nocardiosis are referred to in previous reports.[9,10] In detail, the presence of *Nocardia* infection confirmed by microbiology and/or imaging in 2 or more non-contiguous organs is considered as disseminated nocardiosis. Pulmonary infections related to localized organs or systems are classified as localized nocardiosis. Nocardia was considered a colonizer if all 4 of the following conditions were met simultaneously:[11] (1) Nocardia was isolated from a nonsterile site; (2) either the patient had no clinical symptoms consistent with Nocardia infection or an alternative diagnosis was present to explain the initial symptoms; (3) patient did not receive antibiotic treatment at a dose and duration (at least 4 months) recommended for invasive nocardiosis; and (4) the clinical presentation did not change during the follow-up period to warrant a revised diagnosis of invasive nocardiosis. In the present study, cases meeting the above criteria for colonization have been excluded.

Statistical Analysis

Excel 2019 was used to manage all the data, and statistical analysis was conducted using SPSS 25.0 (SPSS Inc., Chicago, United States) software. Regarding comparisons between groups, the Student's *t*-test or Wilcoxon test was used for analysis of continuous data, while the chi-square test or Fisher's exact probability for analysis of categorical data. $P<0.05$ was deemed to be statistically significant.

Results

Baseline Characteristics

After screening, a total of 77 cases were involved and 23 cases were then excluded due to lack of information, finally 54 cases were included in this study. Of the total 54 enrolled patients, 34 were identified as localized nocardiosis, while the remaining 20 were identified as disseminated nocardiosis, according to the criteria. The baseline characteristics of the patients were displayed in Table 1. The mean age of the localized nocardiosis group was 54.0 years, with 55.9% (19/34) males and 44.1% (15/34) females, whilst the mean age of the disseminated nocardiosis group was 44.2 years, with 65.0% (13/20) males and 35.0% (7/20) females. Notably, patients with disseminated infections were more prone to receive long-term glucocorticoids and/or immunosuppressants than the localized nocardiosis group ($P=0.027$). Furthermore, the proportion of patients with chronic structural lung disease was higher in the localized infection group ($P=0.010$).

Clinical Manifestations

The prevalent infection sites in the localized nocardiosis group were lung and skin soft tissue, while the prevalent infection sites were lung, central nervous system, and soft skin tissue for disseminated nocardiosis group. Remarkably, disseminated infections were more likely to invade the central nervous system ($P<0.001$), soft skin tissues ($P=0.019$), and

Table 1 The Difference of Clinical Characteristics and Treatment Outcomes Between Localized and Disseminated Nocardiosis

	Total (n = 54)	Outcome [n (%)]		*P*-value
		Localized nocardiosis (n = 34)	Disseminated nocardiosis (n = 20)	
Baseline characteristics				
Age	50.4±18.7	54.0±19.3	44.2±16.4	*P*=0.064
Sex				
Male	32 (59.3)	19 (55.9)	13 (65.0)	*P*=0.510
Female	22 (40.7)	15 (44.1)	7 (35.0)	
Smoke	12 (22.2)	7 (20.6)	5 (25.0)	*P*=0.970
Alcohol	2 (3.7)	0 (0.0)	2 (10.0)	*P*=0.257
Long-term glucocorticoids and/or immunosuppressants	30 (55.6)	15 (44.1)[a]	15 (75.0) [b]	*P*=0.027
Chronic structural lung disease	23 (42.6)	19 (55.9)	4 (20.0)	*P*=0.010
Diabetes	15 (27.8)	10 (29.4)	5 (25.0)	*P*=0.727
Chronic liver disease	8 (14.8)	4 (11.8)	4 (20.0)	*P*=0.670
Tumors or blood disease	2 (3.7)	2 (5.9)	0 (0.0)	*P*=0.747
Infection site				
Lung	41 (75.9)	23 (67.6)	18 (95.0)	*P*=0.127
Central nervous system	13 (24.1)	0 (0)	13 (65.0)	*P*<0.001
Skin soft tissue	19 (35.2)	8 (23.5)	11 (55.0)	*P*=0.019
Bone tissue	4 (7.4)	0 (0.0)	4 (20.0)	*P*=0.030
Eye	2 (3.7)	1 (2.9)	1 (5.0)	*P*>0.999
Else tissue	8 (14.8)	2 (5.9)	6 (30.0)	*P*=0.044

(*Continued*)

Table 1 (Continued).

	Total (n = 54)	Outcome [n (%)]		*P*-value
		Localized nocardiosis (n = 34)	Disseminated nocardiosis (n = 20)	
Clinical manifestations				
Fever	43 (79.6)	24 (70.6)	19 (95.0)	*P*=0.072
Cough and expectoration	36 (66.7)	22 (64.7)	14 (70.0)	*P*=0.690
Ecphysesis	16 (29.6)	12 (35.3)	4 (20.0)	*P*=0.235
Hemoptysis	8 (14.8)	4 (11.8)	4 (20.0)	*P*=0.670
Chest pain	7 (13.0)	5 (14.7)	2 (10.0)	*P*=0.938
Septic shock	6 (11.1)	3 (8.8)	3 (15.0)	*P*=0.803
Skin and soft tissue lesions	19 (35.2)	8 (23.5)	11 (55.0)	*P*=0.019
Headaches	7 (13.0)	0 (0.0)	7 (35.0)	*P*=0.001
Impaired neurological function	7 (13.0)	0 (0.0))	7 (35.0)	*P*=0.001
Epilepsy	3 (5.6)	0 (0.0)	3 (15.0)	*P*=0.088
Other symptoms	9 (16.7)	6 (17.6)	3 (15.0)	*P*=0.900
Radiological features (chest CT imaging)				
Pulmonary nodules	30 (55.6)	15 (44.1)	15 (75.0)	*P*=0.027
Patchy shadows	33 (61.1)	22 (64.7)	11 (55.0)	*P*=0.480
Cavernous shadows	22 (40.7)	11 (32.4)	11 (55.0)	*P*=0.102
Solid shadows	17 (31.5)	8 (23.5)	9 (45.0)	*P*=0.101
Bronchial dilatation	15 (27.8)	13 (38.2)	2 (10.0)	*P*=0.025
Pleural effusion	14 (25.9)	9 (26.5)	5 (25.0)	*P*=0.905
Treatment				
Monotherapy	10 (18.5)	10 (29.4)	0 (0.0)	*P*=0.020
Combined therapy	44 (81.5)	24 (70.6)	20 (100.0)	
Prognosis[c]				
Hospitalization period	27.0 (15.0, 35.5)	20.0 (14.0, 31.0)	32.5 (25.3, 47.8)	*P*=0.016
Recover	47 (92.2)	28 (90.3)	19 (95.0)	*P*=0.942
Death	4 (7.8)	3 (9.7)	1 (5.0)	

Notes: [a]11 cases of autoimmune diseases (5 cases of systemic lupus erythematosus (SLE), 3 cases of anti-neutrophil cytoplasmic antibodies (ANCA)-associated vasculitis, 1 case each of rheumatoid arthritis with interstitial pneumonia, dermatomyositis, and anti-Jo-1 antibody syndrome), 3 cases of nephrotic syndrome, 1 case of congenital aplastic anemia. [b]9cases of autoimmune diseases (6 cases of SLE, 2 cases of granulomatous/ systemic vasculitis and 1 case of rheumatoid arthritis), 3 cases of nephrotic syndrome, 1 case of IgA nephropathy, 1 case of atypical membranous nephropathy respectively, 1 case of aplastic anemia. [c]2 with pulmonary nocardia and 1 with biliary nocardia, all loss to follow-up. Data labeled in red represent statistically significant (*P*<0.05).

bone tissues (*P*=0.030) compared to localized infections (Table 1). Fever, cough, and expectoration were common symptoms of nocardiosis in both groups. However, patients with disseminated infections were more likely to suffer from headache (*P*=0.001), impaired neurological function (eg, blurred vision, altered visual field, unfavorable speech, limb weakness, etc., *P*=0.001), and soft tissue skin lesions (*P*=0.019).

Radiological Features

In the present study, we revealed that pulmonary nodules were prominent features of chest imaging changes in patients with disseminated infections (*P*=0.027) whereas bronchial dilatation was more common in patients with localized infections (*P*=0.025). In addition, we also found that when *Nocardia* infection affected the central nervous system (CNS), the most common cranial MRI or CT manifestations were brain abscesses: multiple brain abscesses in 53.8% (7/13), single brain abscesses in 23.1% (3/13) and abnormal signals in 23.1% (3/13) of the patients.

Identification and Distribution of Nocardia Species

All the cases included in this study had positive culture results for *Nocardia* species. In localized nocardiosis, 13 specimens were positive for both weakly acid-fast staining and culture and 21 were positive for culture only, whereas in disseminated nocardiosis, 12 specimens were positive for both weakly acid-fast staining and culture and 8 were positive for culture only. In terms of species distribution, the most frequent isolates were *Nocardia farcinica* and *Nocardia brasiliensis*, regardless of localized or disseminated infections (Figure 1). Nevertheless, for localized infections, *Nocardia* is mostly isolated from alveolar lavage fluid (16/34, 47.1%), whereas for disseminated infections, *Nocardia* is most seen in soft skin tissue (11/20, 55.0%, Figure 2).

Treatment and Prognosis

All 54 patients were given anti-*Nocardia* treatment after etiological diagnosis. Among patients with localized infection, 29.4% (10/34) were treated with monotherapy and 70.6% (24/34) with combination therapy, of which 66.6% (16/24) included TMP-SMX. In terms of prognosis, 90.3% (28/31) of the patients recovered, 3 died in hospital and 3 abandoned treatments. For the localized infection group, TMP-SMX is often used in combination with carbapenems, quinolones, minocycline, ceftazidime, amikacin, and linezolid. Notably, combination therapy was used in all the patients with disseminated nocardiosis (20/20), of which 85.0% (17/20) were treated based on TMP-SMX in combination with 1–2 other antibiotics such as carbapenems, quinolones, tetracyclines, cephalosporins, aminoglycosides and oxazolidinones. Eventually, 95.0% (19/20) of the patients recovered and 1 patient was discharged spontaneously. It is worth noting that the average hospitalization days were significantly longer for those with disseminated infection (32.5 days) than those with localized infection (20.0 days, P=0.016, Table 1).

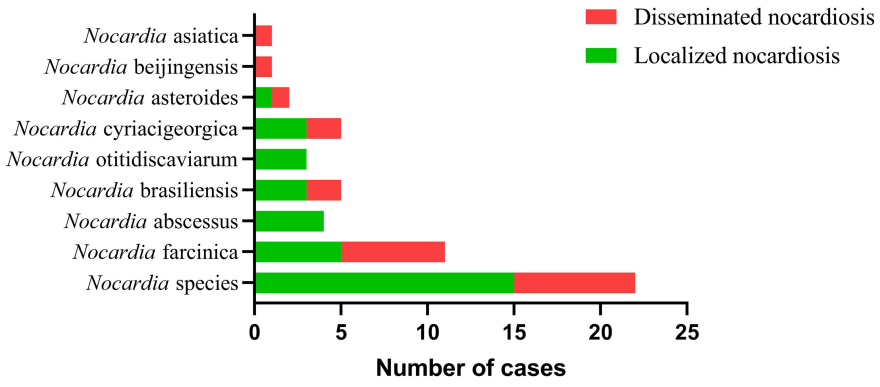

Figure 1 The identification results of *Nocardia* species in this study.

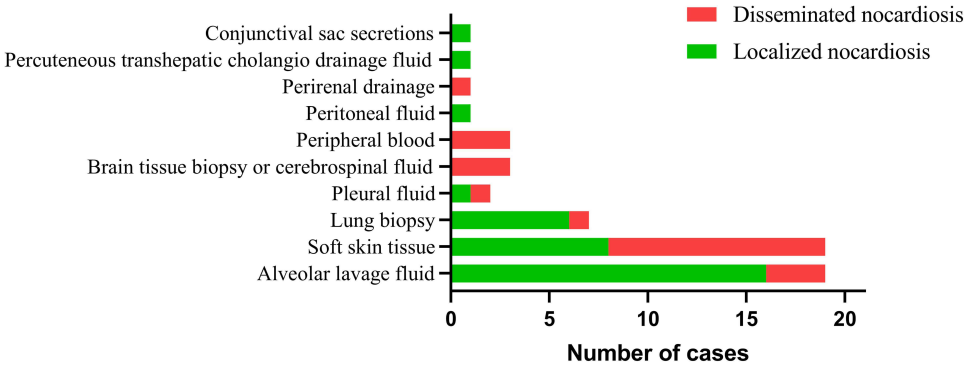

Figure 2 Sample distribution of *Nocardia* species in this study.

Discussion

An important finding of this study is that disseminated nocardiosis was more common in hosts on long-term glucocorticoid and/or immunosuppressive agents, with the most common species being *Nocardia farcinica*. The role of disseminated nocardiosis in populations with immunosuppressed conditions has been extensively explored. Soueges et al also demonstrated that hosts with autoimmune diseases, high doses of corticosteroid therapy, lymphopenia or *Nocardia farcinica* infection were more likely to develop disseminated infections.[10] In the study by Zachary A Yetmar et al, all 33 solid organ transplant recipients had pulmonary involvement, and the majority of patients had central nervous system involvement.[12] They also revealed that 24.2% (8/33) patients with disseminated infection died within 12 months of diagnosis compared to 14.1% (13/92) of patients without disseminated infection. An autopsy study in West Africa showed that 10 of 247 adult HIV cadavers had pulmonary nocardiosis, of which 6 showed disseminated disease.[13] Thus, we hypothesize that immunosuppressed populations are more likely to develop disseminated disease due to their lowered immunity. Meanwhile, this group needs to be given adequate attention due to the risk of potential poor outcomes. We also found that patients with chronic structural lung disease were mainly associated with localized nocardiosis. For patients with chronic structural lung disease, altered ciliary motility and epithelial damage in the lower respiratory tract may facilitate the survival of *Nocardia*.

The lung was the most common infection site in this study for both disseminated and localized nocardiosis. In particular, localized infections primarily appear in populations with chronic structural lung disease, and disseminated infections involving the lung mostly occur in patients taking long-term glucocorticoids and/or immunosuppressive agents. The clinical manifestations of pulmonary nocardiosis are mainly fever, cough and expectoration, shortness of breath, and imaging changes may show patchy, nodular, cavernous, or bronchial dilatation, etc. From this perspective, the clinical presentation and imaging changes of nocardiosis were not specific and could easily lead to misdiagnosis. Hence, in patients presenting with unexplained pulmonary symptoms, pathogenic testing for *Nocardia* is necessary to rule out misdiagnosis and delayed treatments. This study revealed that when *Nocardia* infection involved the CNS, both brain abscesses and abnormal signals were observed. CNS involvement predominantly occurs in immunocompromised populations and the most common imaging presentation is brain abscess.[14] Primary cutaneous nocardiosis has been reported to be more common in immunocompetent individuals.[15] The clinical presentation of cutaneous nocardiosis is similar to that of other skin infections and may present as skin nodules, subcutaneous abscesses, cellulitis and cutaneous lymph vascular syndrome, making it difficult to differentiate between sporotrichosis, tuberculosis, non-tuberculous mycobacteriosis, leishmaniasis and syphilis.[16] We recommend that immunocompromised patients presenting with the above skin lesions could be screened for cutaneous nocardiosis and undergo a skin biopsy.

The most common strains isolated in this study were *Nocardia farcinica* and *Nocardia brasiliensis*, both in disseminated and localized infections. Wang et al analyzed 441 strains of *Nocardia* from 21 provinces/cities in China and revealed that the common strains were *Nocardia farcinica* (39.9%) and *Nocardia cyriacigeorgica* (28.6%).[17] Another study derived from a tertiary hospital in Hunan province showed that the most prevalent species of *Nocardia* isolated in 2018–2019 were *Nocardia farcinica* (81.8%) and *Nocardia nova* (11.4%).[18] In combination with our findings, *Nocardia farcinica* is still predominant, although the distribution of other *Nocardia* species varies from region to region. *Nocardia farcinica* is thought to be closely associated with multiloculated cerebral abscesses, which may lead to significant mortality.[19] Additionally, *Nocardia farcinica* is prone to complications in patients with underlying malignancies or autoimmune diseases, further increasing its aggressiveness.[20] Patients with confirmed *Nocardia farcinica* infection should be given focused attention and prompt antimicrobial susceptibility testing to select appropriate antibiotics, which may help minimize mortality. The most frequent sample types for localized and disseminated infections were alveolar lavage fluid and skin and soft tissue, respectively. Inhalation of dust containing *Nocardia* in the lung or direct inoculation through injury may be an important route of infection for *Nocardia*, especially in immunocompromised individuals.[21] It has also been reported that 32% of recipients of solid organ transplants with nocardiosis have skin lesions.[22] For this reason, pathogenic diagnosis can be applied to alveolar lavage fluid or skin lesion tissue in patients with suspected nocardiosis.

In a retrospective study conducted by Ercibengoa et al, it was confirmed that there was no statistical difference in 1-year mortality between patients with pulmonary nocardiosis receiving TMP-SMX monotherapy (35%, 8/23) and those receiving other regimens (TMP-SMX-based combination) (41%, 13/32).[23] Margalit et al suggested monotherapy for most patients with localized infections, such as primary cutaneous nocardiosis or non-severe pulmonary nocardiosis whist a combination regimen for severe nocardiosis.[15] As for drug selection, TMP-SMX is the first choice for *Nocardia*. Alternative options such as carbapenems, quinolones, and minocycline are available for patients who are allergic, resistant, or contraindicated to TMP-SMX. Wang et al studied the resistance profile of *Nocardia* from 2009 to 2021 in China and found that all *Nocardia* strains were susceptible to linezolid, followed by amikacin (99.3%) and TMP-SMX (99.1%), with resistance to other antibiotics varying greatly among *Nocardia* species.[17] Given that the resistance rate of *Nocardia* may be increasing, it is advised to perform strain identification and antimicrobial susceptibility testing before using antibiotics in clinical practice. In the localized group, 10 individuals were prescribed monotherapy, while 24 were given combined therapy. All monotherapy-treated patients survived, most of them (6/10) with soft-tissue skin infections. For the combination group, 3 of the 24 patients eventually died. Reports on treatment options for patients with localized nocardiosis are limited. Nso et al reported a case of localized pulmonary *Nocardia farcinica* infection in a 37-year-old male HIV patient, and trimethoprim-sulfamethoxazole was started for pulmonary infection, in addition to antiretroviral therapy.[24] Kogure et al reported a 60-year-old Japanese woman with refractory localized pulmonary nocardiosis caused by *Nocardia mexicana*, and the combination of multi-drug medication and surgery was effective for treating the nocardiosis.[25] Consequently, for localized nocardiosis, various regimes should be selected and adapted to the patient's individual condition to obtain the best therapeutic outcomes. In addition, our study showed that the overall morbidity and mortality rate was not statistically significant in the disseminated infection group compared to the localized infection group possibly because combined and extended anti-infective treatment (TMP-SMX-based combined with 1 to 2 intravenous doses) were applied in the former group.

This study also has some limitations. As a retrospective study, the data collected may have underestimated morbidity and mortality, particularly in patients presenting as mild symptoms and those who did not have a comprehensive examination. Moreover, the limited sample size in this study may hinder the validity of the findings. Future collaborative multi-center studies would help to fully understand the current prevalence, diagnosis, and treatment of nocardiosis in China. Moreover, since this study was a retrospective study with a long-time span, much detailed information could not be given, such as the application of antibiotics after hospital discharge and treatment date. And we were only able to perform a cursory follow-up analysis of the patients through their medical records.

In summary, there were differences in the clinical profiles between patients with localized and disseminated nocardiosis in terms of clinical presentation, infection site, radiological features, treatment, and prognosis. We found that patients with disseminated infections were more prone to receive long-term glucocorticoids and/or immunosuppressants than the localized nocardiosis group. In addition, the disseminated group had longer average hospitalization days relative to the localized group, but there was no significant difference in mortality between them. These findings may provide references for the management and treatment of patients with nocardiosis.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding authors on reasonable requests.

Ethical Approval

The Ethics Committee of Peking Union Medical College Hospital granted a waiver for patient consent, given that the study neither involved the collection of personal privacy information nor subjected participants to any interventions (The Ethical Approve Number: I-23PJ247). The study was conducted in accordance with the Declaration of Helsinki, data were anonymized, and the confidentiality of patients was guaranteed.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors have no relevant financial or non-financial interests to disclose.

References

1. Wilson JW. Nocardiosis: updates and clinical overview. *Mayo Clin Proc*. 2012;87(4):403–407. doi:10.1016/j.mayocp.2011.11.016
2. Mehta HH, Shamoo Y. Pathogenic Nocardia: a diverse genus of emerging pathogens or just poorly recognized? *PLoS Pathog*. 2020;16(3):e1008280. doi:10.1371/journal.ppat.1008280
3. Tremblay J, Thibert L, Alarie I, Valiquette L, Pépin J. Nocardiosis in Quebec, Canada, 1988–2008. *Clin Microbiol Infect*. 2011;17(5):690–696. doi:10.1111/j.1469-0691.2010.03306.x
4. Saubolle MA, Sussland D. Nocardiosis: review of clinical and laboratory experience. *J Clin Microbiol*. 2003;41(10):4497–4501. doi:10.1128/JCM.41.10.4497-4501.2003
5. Cattaneo C, Antoniazzi F, Caira M, et al. Nocardia spp infections among hematological patients: results of a retrospective multicenter study. *Int J Infect Dis*. 2013;17(8):e610–614. doi:10.1016/j.ijid.2013.01.013
6. Zhao P, Zhang X, Du P, Li G, Li L, Li Z. Susceptibility profiles of Nocardia spp. to antimicrobial and antituberculotic agents detected by a microplate Alamar Blue assay. *Sci Rep*. 2017;7:43660. doi:10.1038/srep43660
7. Yasuike M, Nishiki I, Iwasaki Y, et al. Analysis of the complete genome sequence of Nocardia seriolae UTF1, the causative agent of fish nocardiosis: the first reference genome sequence of the fish pathogenic Nocardia species. *PLoS One*. 2017;12(3):e0173198. doi:10.1371/journal.pone.0173198
8. Brown-Elliott BA, Biehle J, Conville PS, et al. Sulfonamide resistance in isolates of Nocardia spp. from a US multicenter survey. *J Clin Microbiol*. 2012;50(3):670–672. doi:10.1128/JCM.06243-11
9. Restrepo A, Clark NM. Nocardia infections in solid organ transplantation: guidelines from the infectious diseases community of practice of the American society of transplantation. *Clin Transplant*. 2019;33(9):e13509. doi:10.1111/ctr.13509
10. Soueges S, Bouiller K, Botelho-Nevers E, et al. Prognosis and factors associated with disseminated nocardiosis: a ten-year multicenter study. *J Infect*. 2022;85(2):130–136. doi:10.1016/j.jinf.2022.05.029
11. Dumitrascu AG, Rojas CA, Stancampiano F, et al. Invasive nocardiosis versus colonization at a tertiary care center: clinical and radiological characteristics. *Mayo Clin Proc Innov Qual Outcomes*. 2023;7(1):20–30. doi:10.1016/j.mayocpiqo.2022.11.002
12. Yetmar ZA, Challener DW, Seville MT, Bosch W, Beam E. Outcomes of nocardiosis and treatment of disseminated infection in solid organ transplant recipients. *Transplantation*. 2023;107(3):782–791. doi:10.1097/TP.0000000000004343
13. Lucas SB, Hounnou A, Peacock C, Beaumel A, Kadio A, De Cock KM. Nocardiosis in HIV-positive patients: an autopsy study in West Africa. *Tuber Lung Dis*. 1994;75(4):301–307. doi:10.1016/0962-8479(94)90137-6
14. Meena DS, Kumar D, Bohra GK, Midha N, Garg MK. Clinical characteristics and treatment outcome of central nervous system nocardiosis: a systematic review of reported cases. *Med Princ Pract*. 2022;31(4):333–341. doi:10.1159/000525509
15. Margalit I, Lebeaux D, Tishler O, et al. How do I manage nocardiosis? *Clin Microbiol Infect*. 2021;27(4):550–558. doi:10.1016/j.cmi.2020.12.019
16. Ramos ESM, Lopes RS, Trope BM. Cutaneous nocardiosis: a great imitator. *Clin Dermatol*. 2020;38(2):152–159. doi:10.1016/j.clindermatol.2019.10.009
17. Wang H, Zhu Y, Cui Q, et al. Epidemiology and antimicrobial resistance profiles of the nocardia species in China, 2009 to 2021. *Microbiol Spectr*. 2022;10(2):e0156021. doi:10.1128/spectrum.01560-21
18. Li J, Shen H, Yu T, et al. Isolation and characterization of nocardia species from pulmonary nocardiosis in a tertiary hospital in China. *Jpn J Infect Dis*. 2022;75(1):31–35. doi:10.7883/yoken.JJID.2020.1096
19. Beucler N, Farah K, Choucha A, et al. Nocardia farcinica cerebral abscess: a systematic review of treatment strategies. *Neurochirurgie*. 2022;68(1):94–101. doi:10.1016/j.neuchi.2021.04.022
20. Budzik JM, Hosseini M, Mackinnon AC Jr, Taxy JB. Disseminated Nocardia farcinica: literature review and fatal outcome in an immunocompetent patient. *Surg Infect (Larchmt)*. 2012;13(3):163–170. doi:10.1089/sur.2011.012
21. Traxler RM, Bell ME, Lasker B, Headd B, Shieh WJ, McQuiston JR. Updated Review on Nocardia Species: 2006–2021. *Clin Microbiol Rev*. 2022;35(4):e0002721. doi:10.1128/cmr.00027-21
22. Burke VE, Lopez FA. Approach to skin and soft tissue infections in non-HIV immunocompromised hosts. *Curr Opin Infect Dis*. 2017;30(4):354–363. doi:10.1097/QCO.0000000000000378
23. Ercibengoa M, Càmara J, Tubau F, et al. A multicentre analysis of Nocardia pneumonia in Spain: 2010–2016. *Int J Infect Dis*. 2020;90:161–166. doi:10.1016/j.ijid.2019.10.032

24. Nso N, Nassar M, Guzman Perez LM, Shaukat T, Trandafirescu T. Localized pulmonary nocardia farcinica infection as the presenting symptom of acquired immunodeficiency syndrome. *Cureus*. 2021;13(8):e17611. doi:10.7759/cureus.17611
25. Kogure M, Takase E, Fusamoto A, et al. Treatment of refractory localized pulmonary nocardiosis caused by Nocardia mexicana with a combination of medication and surgery. *Respirol Case Rep*. 2023;11(3):e01098. doi:10.1002/rcr2.1098