The Clinical Characteristic and Management of patients with nocardiosis in a tertiary hospital in China

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Research Article

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Abstract

Background

Nocardiosis is an uncommon opportunistic bacterial infection caused by *Nocardia* spp., and its incidence has increased significantly in recent years. This study aimed to summarize the clinical characteristics and management of nocardiosis to provide a reference for clinical diagnosis and treatment.

Methods

This retrospective study was conducted based on the medical records of nocardiosis patients between January 2015 and December 2021 in a tertiary hospital in China.

Results

Overall, 44 patients with nocardiosis were included in this analysis including 26 males and 18 females with a mean age of 50.4 ± 13.2 years. Connective tissue disease (CTD) was the most common underlying disease (16/44). Twenty-six patients were given immunosuppressive therapy. The most frequent infection sites were the lungs (17/44) and skin and soft tissue (8/44). Common symptoms included cough (23/44), expectoration (18/44), fever (15/44), and subcutaneous abscesses (15/44). Average microbiology laboratory detection time was 4.8 days. Twenty-nine patients were managed only with antimicrobial treatment, and 14 patients received both antimicrobial and surgical therapies. Trimethoprim-sulfamethoxazole (TMP-SMX) was the most commonly used antibiotic (31/44). Thirty-five patients were cured or improved, 6 patients were discharged from the hospital due to poor prognosis, and 1 patient died.

Conclusion

Clinicians should be alert to immunocompromised patients, especially those with CTD, and tend to pulmonary or cutaneous infections. Smear microscopic examination and prolonged culture time may aid Nocardia identification. Patients with nocardiosis can be treated with antimicrobials or surgical therapy. TMP-SMX remains the mainstay treatment, and its early and prompt use may improve nocardiosis outcome.

Introduction

Nocardia is a genus Gram-positive bacterium that belongs to aerobic actinomycetes [1]. It is pervasive in soil, fresh air, saltwater, and dust [2]. *Nocardia* was first discovered in 1888 by veterinarian Edmond Nocard [3,4]. Advances in molecular techniques, such as 16S rRNA gene sequencing has allowed the identification

of more than 100 species of *Nocardia* [1,4,5]. Approximately one-third of *Nocardia* species have been recognized as human pathogens, and the most common species are *N. asterioes, N. brasiliensis, N. farcinica, N. abscessus*, and *N. cyricigeorgica* [6,7].

Nocardiosis most frequently involves the lungs, central nervous system (CNS), and skin and can also affect the joints, kidneys, and other organs [8,9]. Several studies have revealed that immunocompromised patients and recipients of solid organ transplants were more susceptible to nocardiosis [1,10].

In recent years, the incidence of nocardiosis has increased significantly, which may be associated with an increasing number of immunocompromised patients and advancements in laboratory detection methods, along with a high mortality rate ranging from 20–30%, so it receives considerable attention from clinicians [11,12]. However, compared with other bacteria, the incidence is still very low. *Nocardia* are infrequent and difficult-to-culture bacteria, which are easily missed and misdiagnosed in the clinic. Moreover, the diagnosis of nocardiosis is difficult, because there are no specific signs and symptoms [13]. Consequently, it is fundamental to increase awareness regarding *Nocardia* identification and the clinical characteristics of nocardiosis. Most of the literature on nocardiosis published in China and abroad includes case reports or small case series, and there have been few systematic analyses of nocardiosis. Marked geographical variability in the distribution of *Nocardia* has also been shown, but in China, such research remains scarce [14]. Here, we retrospectively studied nocardiosis that occurred in the past seven years in a tertiary hospital in China and summarized the clinical characteristics and management of nocardiosis, aiming to provide a reference for early clinical diagnosis, timely treatment, and improving the prognosis of patients.

Material And Methods

Clinical data collection

Data on nocardiosis cases were collected from patients in a tertiary hospital in China from January 2015 to December 2021. Demographic data (including sex, age, and visit time), underlying diseases [connective tissue disease (CTD), hypertension, respiratory disease, and history of immunosuppressive therapy], clinical manifestations (fever, cough, expectoration, subcutaneous abscesses, shortness of breath, muscle soreness, asthenia, altered consciousness, and hemoptysis), laboratory tests [routine blood tests, hepatic and renal function, erythrocyte sedimentation rate, serum C-reactive protein (CRP), and procalcitonin (PCT)], radiological examinations [chest computed tomography (CT) and magnetic resonance imaging], diagnosis, treatment (antimicrobial and surgical management), and outcomes were retrospectively reviewed.

Isolation and identification of *Nocardia*

In this study, all *Nocardia* strains were isolated from clinical specimens. Different types of samples were collected, including sputum, bronchial secretions, bronchoalveolar lavage, skin abscesses, abscess

puncture fluid, wound secretion/pus, blood, cerebrospinal fluid (CSF), brain abscess drainage, ocular secretion, peritoneal effusion, joint fluid, and tissue blocks.

The clinical specimens were prepared for smear microscopic examination, incubated, and cultured on different agar plates simultaneously. When Gram-staining and modified acid-fast staining were positive and filamentous and a branched suspicious bacterium was found, microbiologists would consider prolonging the conventional culture time. *Nocardia* isolates were identified using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (Bruker Daltonik, Bremen, Germany). The specific microbiological examination procedures for the common specimens are shown in Fig. 1.

Case definition

A diagnosis of nocardiosis required at least one positive culture result for each sample, and all patients included in the analysis had complete information. Disseminated nocardiosis occurs when at least two non-contiguous organs are clearly infected with *Nocardia* [15,16].

Results

Demographic characteristic of nocardiosis cases

Forty-four patients (26 men, 18 women) with nocardiosis between January 2015 and December 2021 were included in this study. The mean age was 50.4 ± 3.2 years, ranging from 5 to 75 years old. Only one patient was younger than 20 years, and the majority were older than 45 years (72.7%) (Table 1).

Of the 44 patients, underlying diseases were noted in 36. The most common condition was CTD (16/44), followed by chronic kidney disease (10/44), hypertension (9/44), and diabetes (7/44) (Table 2). Nineteen patients had two or more underlying diseases.

Table 2
The demographic and clinical characteristics of patients with nocardiosis cases

Variables	Nocardiosis cases(n = 44)
Age(years), mean ± SD (range)	50.4 ± 13.2
Sex	
Male	26 (59.1%)
Female	18 (40.9%)
Underlying diseases	33 (75.0%)
CTD	16 (36.3%)
Chronic kidney disease	10 (22.7%)
Hypertension	9 (20.5%)
Diabetes	7 (15.9%)
Respiratory disease	5(11.4%)
Viral hepatitis B	5 (11.4%)
CHD	3(6.8%)
Leukemia	2 (4.5%)
Glucocorticoid or immunosuppressive therapy	23 (52.3%)
Clinical characteristics	44(100%)
Cough	23(52.3%)
Expectoration	18(40.9%)
Fever	15(34.1%)
Subcutaneous abscesses	15(34.1%)
Shortness of breath	10 (22.7%)
Headache	7 (15.9%)
muscle soreness	6 (13.6%)
Asthenia	6 (13.6%)
Altered consciousness	4(10.3%)
hemoptysis	4(10.3%)
Chest pain	4(10.3%)
Abbreviations: CTD: Connective Tissue disease; CHD: Coronary heart disease	

Twenty-six patients (59.1%) were treated with glucocorticoids or immunosuppressive therapy, including intravenously administered methylprednisolone and oral prednisolone.

Clinical characteristic of nocardiosis patients

Seventeen patients (38.6%) had pulmonary nocardiosis alone. Involvement of skin and soft tissue was found in 8 patients (18.2%), the CNS was involved in 6 patients (13.6%), and 1 patient (2.3%) presented with an eye infection. Twelve patients (27.3%) presented disseminated nocardiosis, including 6 patients with bloodstream infection, 4 patients with lung, skin, and soft tissue infection, and 2 patients with lung and intraperitoneal infections. The distribution of infection sites is shown in Fig. 2.

The clinical manifestations varied widely. Cough was noted in 23 patients (52.3%), expectoration in 18 patients (40.9%), fever in 15 patients (34.1%), subcutaneous abscesses in 15 patients (34.1%), shortness of breath in 10 patients (22.7%), headache in 7 patients (15.9%), muscle soreness in 6 patients (13.6%), asthenia in 6 patients (13.6%), altered consciousness and hemoptysis in 4 patients each (10.3%) (Table 2).

Isolates and Nocardia **species identification**

Nocardia strains were isolated from 54 specimens, including sputum or bronchial secretions (n = 16), bronchoalveolar lavage (n = 6), skin abscesses or abscess puncture fluid (n = 11), wound secretions or pus (n = 7), blood (n = 6), CSF or brain abscess drainage (n = 3), and others (n = 4). The average time taken for microbial detection was 4.8 days. Twenty-four specimens required more than 4.8 days, and 11 specimens required more than 7 days.

Among the 44 *Nocardia* isolates, only 30 were identified beyond the genus level. The most common species isolated were *N. farcinica* (n = 9, 20.5%), *N. cyricigeorgica* (n = 8, 18.2%), *N. brasilliensis* (n = 3, 6.8%), *N. asteroides* (n = 2, 4.6%), *N. abscessus* (n = 2, 4.6%), *N. nova* (n = 2, 4.6%), *N. araoensis* (n = 2, 4.6%), *N. otitidiscaviarum* (n = 1, 2.3%), *N. pseudobrasiliensis* (n = 1, 2.3%), and 14 isolates could not be identified at the species level (n = 14, 31.8%) (Fig. 3).

Laboratory tests and radiological examinations

Of 44 patients, 26 patients (59.1%) showed elevated white cells, 30 patients (68.2%) showed elevated neutrophil proportion, and 34 patients (77.3%) showed decreased lymphocyte counts. Serum CRP levels were elevated in 26 patients (59.1%), and PCT levels were increased in 26 patients (59.1%). Twenty patients (45.5%) showed lower hemoglobin levels, and 7 patients (15.9%) showed elevated platelet counts. The level of serum album decreased in 32 patients (72.7%), 28 patients (63.6%) presented with an elevated ECR, and 9 patients (20.5%) had elevated serum creatinine (Table 1).

Bilateral involvement was detected in the chest CT images of 34 patients (77.3%), and 4 patients (9.1%) had unilateral involvement. All pulmonary nocardiosis cases showed abnormal chest CT findings. The

most common radiological findings were nodules (38.6%), pleural effusion (15.9%), and patchy shadows (15.9%). Other imaging findings, such as cavities (11.4%), stripe-shape (11.4%), and mediastinal lymph node enlargement (9.1%) were relatively rare. Among the 6 cases of CNS infection, 5 patients had intracranial space-occupying lesions, and 1 patient showed cerebral atrophy in magnetic resonance imaging.

Management and outcome

Except for 1 patient who had no clear medication, 29 patients were managed only using antimicrobial treatment, and 14 patients received both antimicrobial and surgical therapy.

Three patients (6.8%) were treated with simple trimethoprim-sulfamethoxazole (TMP-SMX), and 28 patients (63.6%) had received other antibiotics in combination. The antimicrobial agents included oxazolidinones (linezolid), carbapenems (imipenem and meropenem), quinolones (moxifloxacin and levofloxacin), cephalosporins (ceftriaxone and cefoperazone-sulbactam), and aminoglycosides (amikacin). The remaining 12 patients were administered one or more antibiotics.

Thirty-six patients were cured or improved, 5 were discharged from the hospital due to serious illness or poor prognosis, 2 outpatients lost follow-up, and 1 patient died. In addition, 2 patients experienced relapse, 1 of whom was cured, and another patient died.

The specific times for diagnosis, therapy, and disease duration are shown in Table 1.

Discussion

This is one of the largest contemporary single-center retrospective studies to describe the clinical characteristics and management of 44 patients with nocardiosis in China. Nocardiosis mainly occurs in middle-aged and elderly men, and it is frequently complicated by a series of underlying diseases [8,17,18]. Unlike other studies that reported chronic lung diseases as the most common underlying diseases, our findings suggest that clinicians treating immunocompromised patients, especially those with CTDs, should be vigilant of nocardiosis [14,19]. CTD patients who were taking either glucocorticoids or immunosuppressive drugs were the most common nocardiosis subjects at our institution, and the infection sites were dominated by the lungs and skin. A retrospective study from Israel showed that immunosuppressive drug therapy was positively correlated with nocardiosis [20].

Isolation and culture are the principal methods for diagnosis of nocardiosis [21]. At present, isolation of *Nocardia* on common or selective media usually takes 2–7 days, which causes a delay in diagnosis [22,23]. Some *Nocardia* strains even need between 1–4 weeks to generate available results, because they require strict culture conditions and have a slow growth rate at 35°C in standard culture medium; the presence of normal flora or treatment with antimicrobial therapy would also affect *Nocardia* culture [11,13,14,24,25]. In our study, the average time for microbial detection was 4.8 days, and 11 specimens required more than 7 days, which exceeded the conventional culture time (≥ 2 days). Hence, on one hand, clinicians should

inform microbiologists of suspicious cases and require more attention to these specimens if possible. On the other hand, during common culture time, the smear microscopic examination (Gram staining and modified acid-fast staining) revealed a Gram-positive, filamentous, and partially acid-fast branched bacterium suspected to be *Nocardia*. This alerted microbiologists that prolonged the normal culture time and continued observation. A previous study of confirmed nocardiosis patients also demonstrated that Gram staining was a sensitive method for recognizing *Nocardia* in clinical specimens [22]. Thus, smear microscopic examination is a necessary adjunct to avoid missing detections and improve detection rate.

Ten Nocardia species were identified among the 44 isolates. *N. farcinica* (20.5%) was the most common species, followed by *N.cyricigeorgica* (18.2%) and *N.brasilliensis* (6.8%). The distribution of *Nocardia* showed recognizable geographical variation. In other case series, the most frequently isolated *Nocardia* were diverse, including *N. cyricigeorgica* in Australia [14], *N. cyricigeorgica* in Japan [26], *N. brasiliensis* in Taiwan [15] and *N. nova* in the United States [27]. Moreover, a French retrospective analysis suggested that distribution may change over time, which has been reported for the increasing *N. farcinica* proportion from 2010 (13%) to 2014 (27.6%) [28]. Therefore, changes in *Nocardia* distribution must be monitored over time and region.

Clinical symptoms and radiological findings may play an important role in the diagnosis of nocardiosis. In this study, the lungs and skin were the most prevalent sites. Respiratory symptoms, detailed skin examination, and chest CT could be beneficial to clinicians in identifying the infection site [8]. Cough, expectoration, fever, and subcutaneous abscesses were the main clinical presentations, and the most frequent imaging findings were nodules and pleural effusions. CNS infection could present with brain abscesses, and the frontal and parietal regions were commonly affected. Moreover, some inflammatory parameters, including leukocytes, neutrophils, CRP, and PCT, possess a certain reference value. However, these indicators lack specificity and are usually indistinguishable from other bacterial infections, such as tuberculosis and fungal infections [22,29].

Nocardiosis management depends on infection location, disease severity, and host immune status, including surgical debridement or drainage, antibiotic therapy, and improvement of immune function [12]. For patients with abscesses, surgical debridement or drainage of the abscess may complement treatment and help microbiologists and clinicians make definitive diagnoses from postoperative specimens. Before a definite diagnosis, physicians often choose empirical antimicrobial coverage without considering nocardiosis in the initial diagnosis [30]. Among the 44 patients, approximately 47.7% of patients received empirical antimicrobial therapy before the culture results were available. However, empirical treatments were rarely successful in those cases, which may have influenced the culture results and delayed appropriate treatment.

TMP-SMX is the drug of first choice for nocardiosis, and most *Nocardia* spp. are susceptible to this regimen [26,31].We observed that after obtaining the bacterial culture results, clinicians usually changed medication and prescribed TMP-SMX. Currently, there is a trend towards increased resistance to TMP-

SMX. One retrospective evaluation study in the USA from 1995 to 2004 showed a TMP-SMX resistance rate of 42% [27]. Another report from Spain in 2011 described 16.1% resistance to TMP-SMX [32]. Therefore, for TMP-SMX-resistant, disseminated, or severe nocardiosis a combination of TMP-SMX with other antibiotics is recommended [22]. According to the Sanford Guide to Antimicrobial Therapy 2018 [33], TMP-SMX was recommended for cutaneous nocardiosis. In lung and CNS infections, the primary treatment option was TMP-SMX with imipenem, and amikacin addition was considered in disseminated nocardiosis patients. Linezolid is an appealing alternative, because it has high bioavailability, and most *Nocardia* show susceptibility [34]. Other alternative treatment options include minocycline, amikacin, and meropenem [16]. In terms of treatment, 3 months is recommended for immunocompetent patients, at least 6 months for immune-compromised patients, and at least a year for patients with CNS involvement [7]. It has been reported that longer therapy duration may be preferable to prevent recurrence [30]. In our study, nocardiosis management was approximately the same as that of the above therapy, but based on prior treatment experience, the co-medications were slightly different. Doxycycline, tigecycline, moxifloxacin, and ceftriaxone are also commonly used co-medications.

Furthermore, it is noteworthy that individual patients who had taken TMX-SMX could suffer from side effects, which occur frequently due to the long treatment duration [12]. The most common side effects reported by the patients in this study were mainly gastrointestinal symptoms, such as nausea and vomiting, and no patient showed more serious side effects, such as bone marrow suppression or agranulocytosis. When patients could tolerate side effects, dose adjustment was recommended. If side effects were too frequent or severe, the medication was changed to carbapenem, tetracyclines, or other alternative antimicrobial agents.

In the present study, 6 patients died or decided to abandon therapy. In cases with poor prognosis, all patients had underlying diseases, 5 patients used immunosuppressants, 4 of which had CTDs. The disease durations were often long, and the patients received many empirical treatments in upfront therapy. Due to the low incidence, most clinicians did not suspect that the abnormal clinical characteristics of these patients were caused by *Nocardia* in the early stage. Combined with culture difficulty and length, this often caused late diagnosis of nocardiosis and TMX-SMX use. Therefore, it is possible that earlier diagnosis, administration, or prophylactic administration prior to established infection would be beneficial [31].

Our study had some limitations. First, it was a single-center study, and the characteristic features might only represent a limited region; thus, it could be further validated by multicenter studies in the future. Second, as this was a retrospective study, some information, such as outpatient history, was incomplete during clinical data collection. Third, antimicrobial susceptibility tests were not performed in this study.

Conclusion

Clinicians should be alert to immunocompromised patients, especially those with CTDs, and attribute great importance to pulmonary and cutaneous infections. Nocardiosis should be considered when

immunocompromised patients develop respiratory symptoms, fever, abnormal laboratory indicators, radiographic changes, or when empirical anti-infection treatment is suboptimal. At the same time, the communication between clinicians and microbiology laboratories should be enhanced in highly suspicious cases, and microbiologists could use smear microscopic examination and prolong cultivation time to increase *Nocardia* detection rate and make an accurate diagnosis. Patients with nocardiosis can be treated with antimicrobials or surgical therapy. TMP-SMX remains the mainstay of treatment, and its early and prompt use may improve the outcome of nocardiosis. Hence, improving the ability to diagnose nocardiosis and selecting appropriate antimicrobial and surgical treatments is of particular importance to achieve favorable prognosis.

Declarations

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Authors' contributions

Proposed and directed the study□XL,WL; Data collection: PL, ZJ and YL; Prepared the first draft: PL;Revised the manuscript: WL, PL, ZW, XL, QY, BZ. All authors read and approved the final draft of the manuscript.

Availability of data and materials

No applicable

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Ethical approval

Informed consent was not obtained, because this study was retrospective and did not require additional medical procedures. This study was approved by the Ethics Committee of Xiangya Hospital, Central South University.

Consent for Publication

All authors confirm that the details of any images/recordings can be published.

Disclosure

The author reports no conflicts of interest in this work.

References

1. Nakamura I, Nagakura T, Fujita H, Fukusima S, Gonoi T. Nocardia elegans infection: a case report and literature review. Int J Infect Dis. 2017;54:15–17.
2. Wilson JW. Nocardiosis: updates and clinical overview. *Mayo Clin Proc.* 2012;87(4):403–407.
3. Martinez R, Reyes S, Menendez R. Pulmonary nocardiosis: risk factors, clinical features, diagnosis and prognosis. Curr Opin Pulm Med. 2008;14(3):219–227.
4. Conville PS, Brown-Elliott BA, Smith T, Zelazny AM. The Complexities of Nocardia Taxonomy and Identification. J Clin Microbiol. 2018;56(1).
5. Minero MV, Marin M, Cercenado E, Rabadan PM, Bouza E, Munoz P. Nocardiosis at the turn of the century. Medicine (Baltimore). 2009;88(4):250–261.
6. Carrasco G, Valdezate S, Garrido N, Villalon P, Medina-Pascual MJ, Saez-Nieto JA. Identification, typing, and phylogenetic relationships of the main clinical Nocardia species in spain according to their gyrB and rpoB genes. J Clin Microbiol. 2013;51(11):3602–3608.
7. Jiang Y, Huang A, Fang Q. Disseminated nocardiosis caused by Nocardia otitidiscaviarum in an immunocompetent host: A case report and literature review. Exp Ther Med. 2016;12(5):3339–3346.
8. Corsini Campioli C, Castillo Almeida NE, O'Horo JC, et al. Clinical Presentation, Management, and Outcomes of Patients With Brain Abscess due to Nocardia Species. Open Forum Infect Dis. 2021;8(4):ofab067.
9. Farran Y, Antony S. Nocardia abscessus-related intracranial aneurysm of the internal carotid artery with associated brain abscess: A case report and review of the literature. J Infect Public Health. 2016;9(3):358–361.
10. Chen YC, Lee CH, Chien CC, Chao TL, Lin WC, Liu JW. Pulmonary nocardiosis in southern Taiwan. J Microbiol Immunol Infect. 2013;46(6):441–447.
11. Weng SS, Zhang HY, Ai JW, et al. Rapid Detection of Nocardia by Next-Generation Sequencing. Front Cell Infect Microbiol. 2020;10:13.
12. Agterof MJ, van der Bruggen T, Tersmette M, ter Borg EJ, van den Bosch JM, Biesma DH. Nocardiosis: a case series and a mini review of clinical and microbiological features. Neth J Med. 2007;65(6):199–202.
13. Brown-Elliott BA, Brown JM, Conville PS, Wallace RJ, Jr. Clinical and laboratory features of the Nocardia spp. based on current molecular taxonomy. Clin Microbiol Rev. 2006;19(2):259–282.
14. Paige EK, Spelman D. Nocardiosis: 7-year experience at an Australian tertiary hospital. Intern Med J. 2019;49(3):373–379.
15. Liu WL, Lai CC, Ko WC, et al. Clinical and microbiological characteristics of infections caused by various Nocardia species in Taiwan: a multicenter study from 1998 to 2010. Eur J Clin Microbiol Infect Dis. 2011;30(11):1341–1347.
16. Margalit I, Lebeaux D, Tishler O, et al. How do I manage nocardiosis? Clin Microbiol Infect. 2021;27(4):550–558.

17. Huang L, Chen X, Xu H, et al. Clinical features, identification, antimicrobial resistance patterns of Nocardia species in China: 2009–2017. Diagn Microbiol Infect Dis. 2019;94(2):165–172.
18. Mari B, Monton C, Mariscal D, Lujan M, Sala M, Domingo C. Pulmonary nocardiosis: clinical experience in ten cases. Respiration. 2001;68(4):382–388.
19. Kudru CU, Kumar A, Chawla K, Minnamreddigari C, Siddalingaiah N, Guddattu V. A ten-year retrospective analysis of nocardiosis in a tertiary care center of South-coastal India. Infez Med. 2021;29(4):600–608.
20. Margalit I, Goldberg E, Ben Ari Y, et al. Clinical correlates of nocardiosis. Sci Rep. 2020;10(1):14272.
21. Fatahi-Bafghi M. Nocardiosis from 1888 to 2017. Microb Pathog. 2018;114:369–384.
22. Saubolle MA, Sussland D. Nocardiosis: review of clinical and laboratory experience. J Clin Microbiol. 2003;41(10):4497–4501.
23. Jiao M, Deng X, Yang H, Dong J, Lv J, Li F. Case Report: A Severe and Multi-Site Nocardia farcinica Infection Rapidly and Precisely Identified by Metagenomic Next-Generation Sequencing. Front Med (Lausanne). 2021;8:669552.
24. Wang A, Xu Q, Wang Y, Liao H. Orbital and intracranial Nocardia farcinica infection caused by trauma to the orbit: a case report. BMC Infect Dis. 2019;19(1):953.
25. Sawai T, Nakao T, Yamaguchi S, et al. Detection of high serum levels of beta-D-Glucan in disseminated nocardial infection: a case report. BMC Infect Dis. 2017;17(1):272.
26. Toyokawa M, Ohana N, Ueda A, et al. Identification and antimicrobial susceptibility profiles of Nocardia species clinically isolated in Japan. Sci Rep. 2021;11(1):16742.
27. Uhde KB, Pathak S, McCullum I, Jr., et al. Antimicrobial-resistant nocardia isolates, United States, 1995–2004. Clin Infect Dis. 2010;51(12):1445–1448.
28. Lebeaux D, Bergeron E, Berthet J, et al. Antibiotic susceptibility testing and species identification of Nocardia isolates: a retrospective analysis of data from a French expert laboratory, 2010–2015. Clin Microbiol Infect. 2019;25(4):489–495.
29. Sah R, Khadka S, Neupane S, et al. Disseminated infection with Nocardia otitidiscaviarum in a patient under steroid therapy. Clin Case Rep. 2020;8(2):369–373.
30. Xu H, Fu B, Xu L, Sun J. Disseminated Nocardiosis with subretinal abscess in a patient with nephrotic syndrome-a case report. BMC Ophthalmol. 2018;18(1):234.
31. Yagishita M, Tsuboi H, Tabuchi D, et al. Clinical features and prognosis of nocardiosis in patients with connective tissue diseases. Mod Rheumatol. 2021;31(3):636–642.
32. Larruskain J, Idigoras P, Marimon JM, Perez-Trallero E. Susceptibility of 186 Nocardia sp. isolates to 20 antimicrobial agents. Antimicrob Agents Chemother. 2011;55(6):2995–2998.
33. Gilbert DN, Chambers HF, Eliopoulos GM, Saag MS, Pavia AT. *The Sanford guide to antimicrobial therapy.* 2018.
34. Tremblay J, Thibert L, Alarie I, Valiquette L, Pepin J. Nocardiosis in Quebec, Canada, 1988–2008. Clin Microbiol Infect. 2011;17(5):690–696.

Tables

Table 1 is available in the Supplementary Files section.

Figures

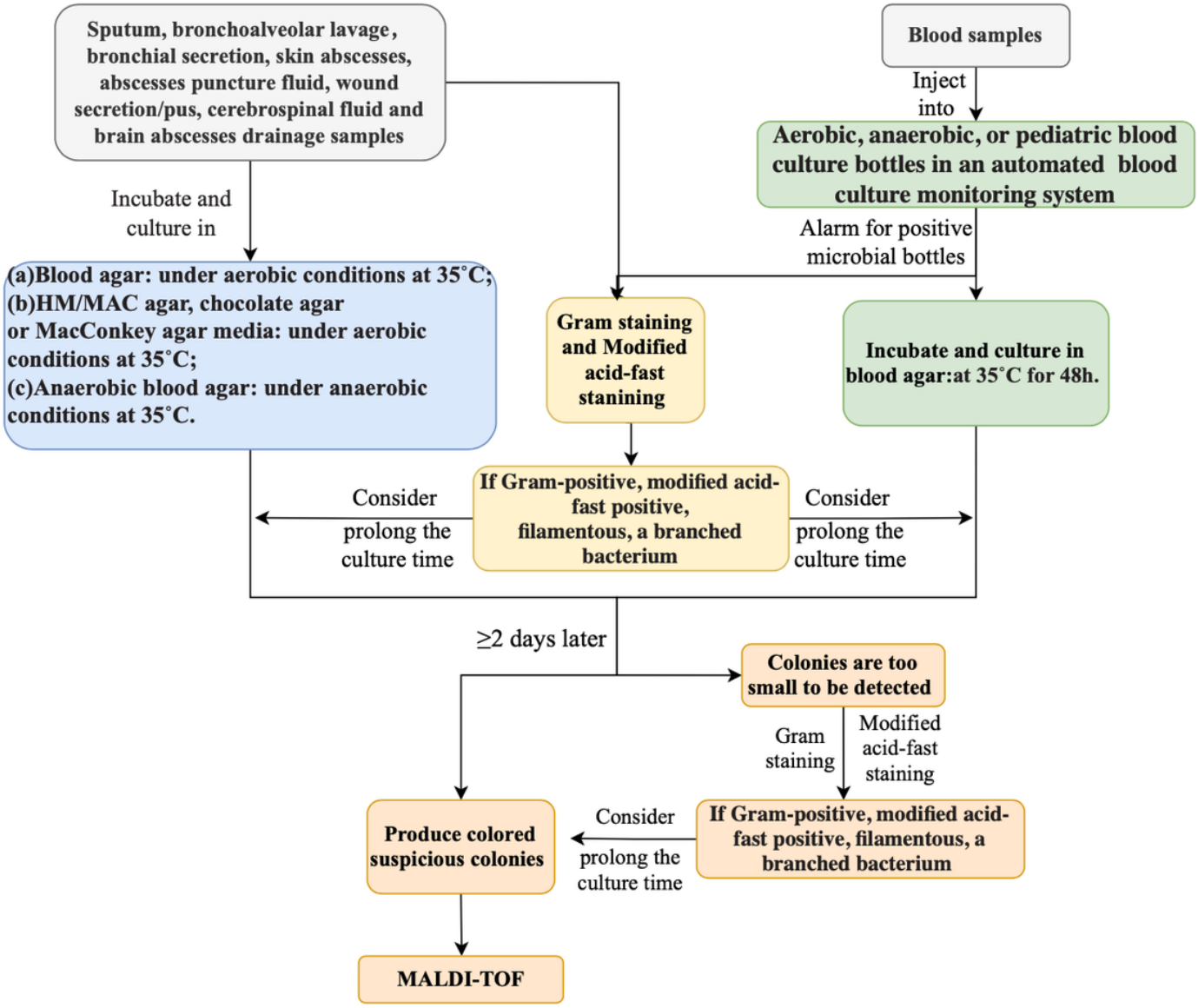

Figure 1

The specific microbiology examinations of common specimen. All *Nocardia* strains were isolated from different clinical specimens. The clinical specimens were prepared for smear microscopic examination, incubated, and cultured on different agar plates simultaneously. *Nocardia* isolates were identified using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry finally.

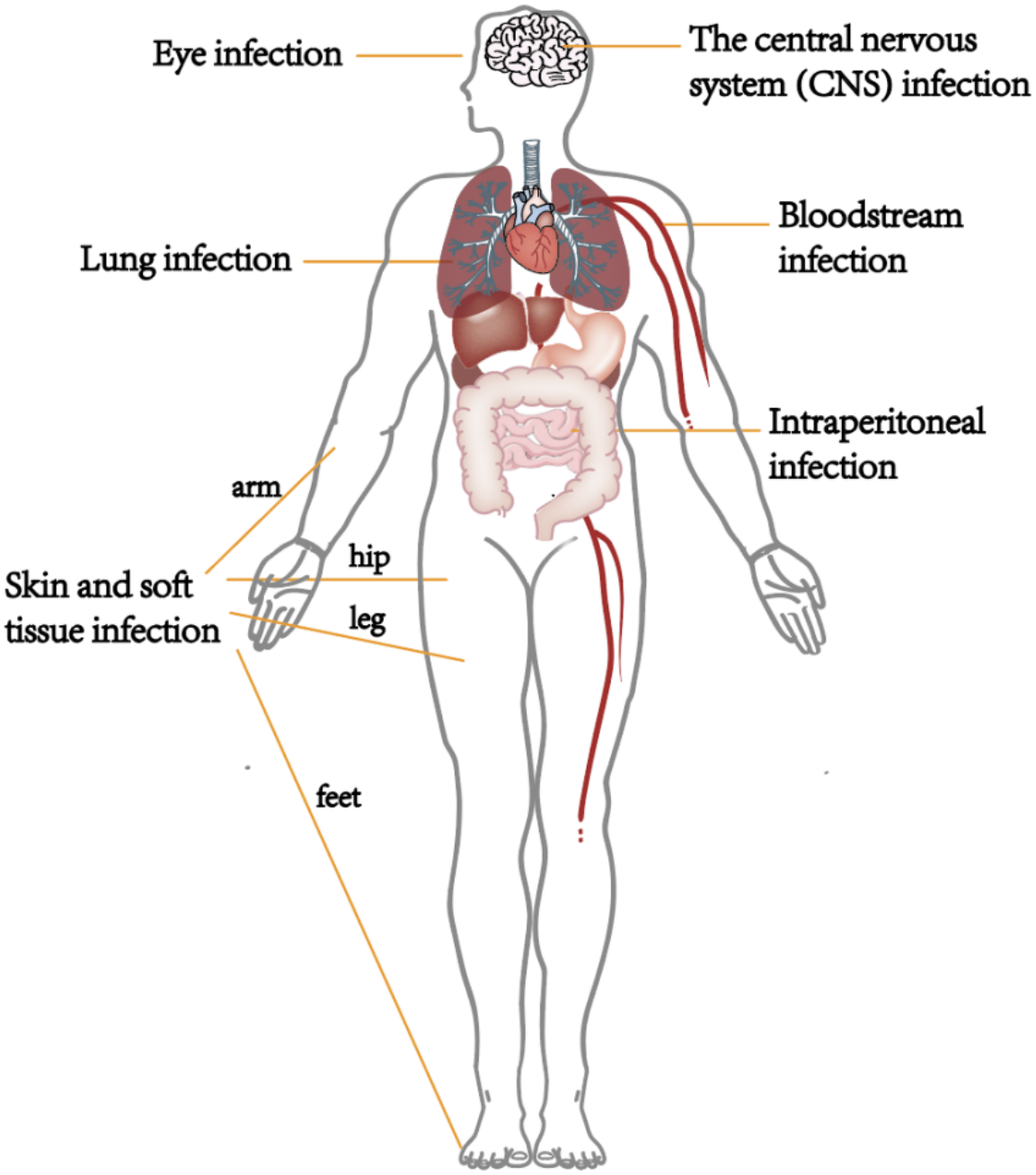

Figure 2

The distribution of infection sites. The most frequent infection sites were the lungs and skin and soft tissue.Twelve patients (27.3%) presented disseminated nocardiosis.

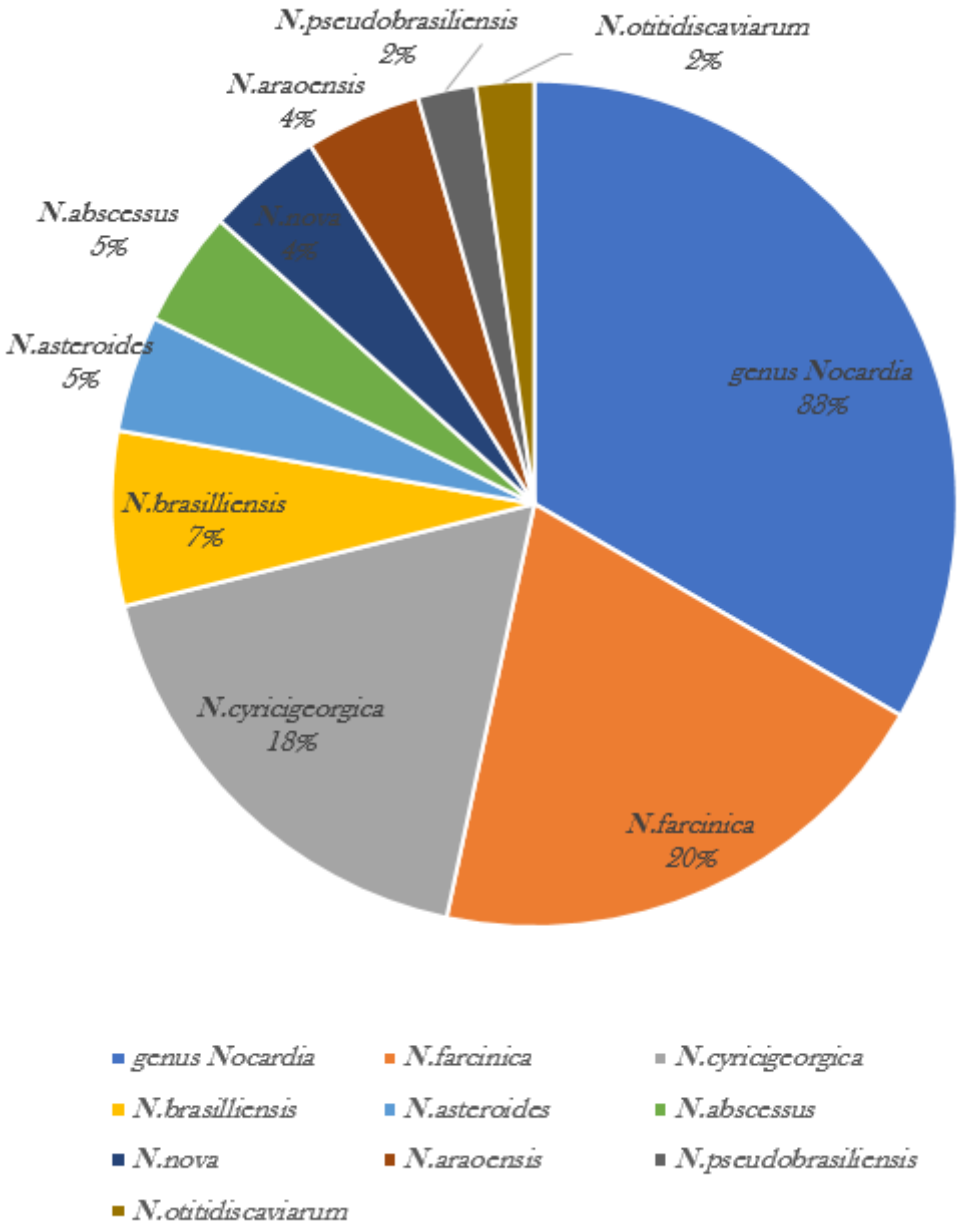

Figure 3

Distribution of *Nocardia spp.* Among the 44 Nocardia isolates, only 30 were identified beyond the genus level. The most common species isolated were *N. farcinica (n=9, 20.5%), N. cyricigeorgica* (n=8, 18.2%), *N. brasilliensis* (n=3, 6.8%), *N. asteroides* (n=2, 4.6%), *N. abscessus* (n=2, 4.6%), *N. nova* (n=2, 4.6%), *N. araoensis* (n=2, 4.6%), *N. otitidiscaviarum* (n=1, 2.3%), *N. pseudobrasiliensis* (n=1, 2.3%), and 14 isolates could not be identified at the species level.

Supplementary Files

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