Original Article

Comparison Of The Clinical Presentation, Antimicrobial Properties, And Outcomes Of Lung And Disseminated Nocardiosis Patients

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Abstract

Introduction: Nocardia are widely distributed in both water and soil. Nocardia is an infectious agent that spreads through injured skin and through respiratory exposure. Diseases of the lungs, skin, subcutaneous tissue, and extensive blood disorders may all be brought on by the organism. Chronic respiratory disease, immunosuppression brought on by steroid hormones or other immunosuppressants, HIV infection, solid organ transplants, and chemotherapy for malignancy are all prevalent risk indicators for Nocardia illnesses. Nocardiosis prevalence has risen in recent decades as a result of strong immunosuppressant drugs.

Objectives: To compare the clinical presentation, antimicrobial properties, and outcomes of lung and disseminated nocardiosis patients.

Methodology: Contributing diseases, participant types with pulmonary and widespread nocardiosis infections, immunosuppressants, the location of the Nocardia isolate, antibacterial treatment, surgical treatment, and the final outcome were all gathered. If blood cultures showed the existence of non-Nocardial microorganisms and the individual exhibited symptoms suggestive of bacteremia, the individual was said to have simultaneous bacteremia. Advancement in clinical signs and drug sensitivity measured in vitro were used to assess the efficacy of antibiotic treatment. Putative Nocardia species samples were placed on slides, treated with acid-fast dye using a modified procedure, and grown on agar media for at minimum two weeks to determine the existence of dominant Gram-positive filamentous microorganisms.Employing common biochemical tests for Nocardia, the isolates were classified down to the species identification. There were 18 participants in this research who had widespread nocardiosis with pulmonary disease. SPSS software version 25 was used for all data analysis. We evaluated the ratios using only a Chi-square test. It was deemed statistically relevant at a 0.05 p-value.

Results: All of the sufferers, the most were male, had an average lifespan of 57.8 years. N. asteroides was primarily accountable for the human disease overall prevalence (44%) whereas N. brasiliensis was in charge of the majority of the disseminated instances (22%). The most prevalent underlying disease was chronic pulmonary disease, which contributed for 17% of occurrences. Cancer contributed for 12% of case scenarios.The form of therapy that was used the most frequently (28%) was the administration of a single medication. In contrast, participants with respiratory and disseminated nocardiosis were much more probable to have illnesses brought on by N. asteroides plus an underlying medical condition, such as malignancy or chronic pulmonary disease.

These people also had clinically urgent conditions, such sepsis, and were frequently first given TB diagnoses when they didn't actually have the illness.

Conclusion: Affected patients received combined antibacterial treatment and immunosuppression medications. Prior to performing a drug sensitivity test, it has been suggested that patients with respiratory or disseminated nocardiosis require standard treatment as an empirical treatment.

Keywords: nocardiosis, outcomes, clinical characteristics, microbiology, lung, disseminated, therapy

Introduction

Aerobic, Gram-positive, beaded, filamentous, mildly acid-fast spreading bacilli of the genus Nocardia are widespread in soil and water (Wilson, 2012). By morphological categorizations, biological approaches, besides 16S ribosomal RNA genetic analysis, more than 100 distinct Nocardia species have been found to far, and above 55 of them have been described as harmful to people (Conville et al., 2018; Cheng et al., 2022).

The opportunistic pathogen Nocardia infects people by ventilation of the lungs and damaged skin. The organism may cause lung, Subcutaneous and superficial cutaneous infections, as well as a widespread blood infection (Wang et al., 2015). Typical causes of Nocardia diseases include chronic lung illness, immunosuppression due to immunosuppressive medications or glucocorticoids, solid organ transplantation, human immunodeficiency virus infection and chemotherapy for cancer (Molina et al., 2018; Zia et al., 2019).

Incidences of nocardiosis have increased in recent years due to severe immunosuppressive medications. Nephrotic syndrome (NS), which is caused by an imbalance in glomerular permeability, is a clinical disease characterised by large proteinuria that leads to hypoalbuminemia (40 g/L), edoema, hyperlipidemia and other consequences. NS patients with impaired renal function, glucocorticoid medication, and immunosuppressant usage may develop immunological problems, rendering them more vulnerable to different infections (Wang et al., 2019).

NS victims undergoing immunosuppressant drugs or long-term adrenal hormones had increased proportions of Nocardiadisease morbidity. Kerbel NC initially discovered a Nocardia disease in NS victims in 1962 (Cheng et al., 2022). There are currently just a deficient of instanceresearches of Nocardiadisease in NS patients, and the dual most recent single-center literature studies were issued in the year 2020. (Guo et al., 2020; Han et al., 2020).

We analysed the clinical features, therapy, antimicrobial susceptibility, and outcomes of hospitalised patients with nocardiosis. The purpose of this study was to compare the clinical presentation, antimicrobial properties, and outcomes of lung and disseminated nocardiosis patients.

Materials and procedures

This research was done at Mardan medical complex from June 2022 to November 2022. Prior to data collection, informed permission was acquired from patients or their family members.

Associated illnesses, participant types with pulmonary and widespread nocardiosis illnesses, immunosuppressants, the location of the Nocardia isolate, antibacterial treatment, medical intervention, and the outcome were all noted. If blood cultures showed the existence of non-Nocardial species and the individual exhibited symptoms suggestive of bacteremia, the patients was said to have simultaneous bacteremia.Within six weeks of a Nocardia-positive culture, glucocorticoid treatment or immunosuppressive therapy were given.Prednisolone 40 mg or even more daily for a period of 1.5 weeks, or 40 mg every day for at least two weeks prior to a positive culture for Nocardia, was considered corticosteroids therapy.The effectiveness of antibiotic treatment was evaluated based on improvement in clinical indications and in vitro antibiotic selectivity. Therapies including a single drug or a combination of agents were also categories for antibacterial drugs regimens.

In order to identify the existence of the most common Gram-positive filamentous microorganisms, samples of suspected Nocardia species were distributed out on slide and labeled with acid-fast using a method described, and cultured on agar plates for at least two weeks. BACTEC blood culture system was used to culture blood. Employing common experimental techniques for Nocardia, such as the breakdown of xanthine, casein, tyrosine and hypoxanthine, the isolates were distinguished down to the genetic level. Minocycline, Amikacin, trimethoprim-sulfamethoxazole (TMP/SMX), cefotaxime, gentamicin, and ampicillin were used for disc diffusion antimicrobial therapy, based on the National Committee for Clinical Laboratory Guidelines.

In this study, there were only 18 individuals with lung involvement and disseminated nocardiosis. Patients with respiratory system and dispersed nocardiosis were categorized with each other to make comparisons of clinical signs, consequences, and antibacterial effects of the excludes with patients with skin problems because respiratory infection and disseminated disease are challenging to distinguish from one another and start sharing more typical clinical and microbiology features.SPSS software version 25 was used for all data analysis. We evaluated the percentages using a Chi-square testing. Statistical significance was determined by a 0.05 meaningful p - value.

Results

Figure 1 shows that the majority of patients were men (n=13) as opposed to females (n=5) based on basic demographic data. The average age and patient microbiological details categorised by kind of illness are shown in Table 1. The standard deviation (SD) was 4.7 years, with the average age being 57.8 years. The following species were identified: N. asteroides (8/18; 44%), N. brasiliensis (6/18; 33%), and N. otitidiscaviarum (3/18; 17%) (table 1). The statistical analysis reveals a statistically significant difference (p=0.03) between the detected Nocardia (N) species. The overall incidence was mostly caused by N. asteroides (44%), but the vast majority of diffused cases were caused by N. brasiliensis (22%).

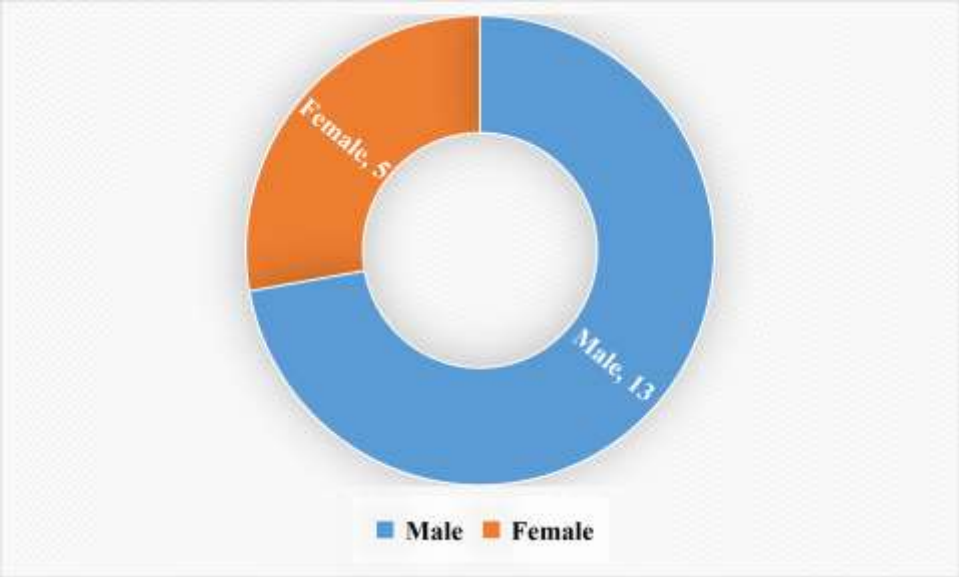


Figure 1. Gender based distribution of patients

Table 1. Participant demographic factors and microbiological information for those with disseminated and pulmonarynocardiosis

Variable	Total	Lung	Disseminated	P-value
Age (mean±SD)	57.8±4.7	51.5±9.2	59.0±11.6	0.27

N. asteroides (n; %)	8; 44%	6; 33%	2; 11%	**0.03***
N. brasiliensis (n; %)	6; 33%	2; 11%	4; 22%	
N. otitidiscaviarum (n; %)	3; 17%	1; 6%	2; 11%	

*P-value is significant (p<0.05)

The most prevalent underlying condition was chronic lung disease (3/18, or 17%), followed by cancer (2/18, or 12%); others included diabetes mellitus (1/18, or 6%), autoimmune disorders (2/18, or 12%), transplantation recipients (0%), and acquired immunodeficiency syndrome (AIDS; 1/18, or 6%). Bronchiectasis, bronchial asthma, and chronic obstructive pulmonary disease comprised chronic lung disease. Cancers included chronic myelocyticleukaemia and one case each of cervical cancer,breast cancer, gingival cancer,rectal cancer, hepatocellular cancer and gastric cancer. Systemic lupus erythematosus, polymyositis, and Paget's disease were autoimmune diseases. The beneficiaries of transplants included kidney, cardiac, and bone marrow transplants. 23% of patients (4/18) got immunosuppressive medication, while 11% of patients (2/18) received corticosteroid therapy (table 2). Localized pulmonary nocardiosis was related with the greatest prevalence of concurrent bacteremia (6%), TB misdiagnosis (6%), and sepsis (6%). 0% of the pulmonary group members were co-infected with TB (table 2).

Table2. Clinical characteristics of the patients

Variable	Total	Lung	Disseminated	P-value
	n (%)	n (%)	n (%)	
Chronic lung disease	3 (17%)	0	3 (17%)	**<0.05***
Diabetes mellitus	1 (6%)	1 (6%)	0	0.35
Malignancy	2 (12%)	1 (6%)	1 (6%)	**<0.05***
Autoimmune disease	2 (12%)	0	2 (12%)	0.61
Transplantation	0	0	0	0.44
AIDS	1 (6%)	0	1 (6%)	0.19
Immunosuppressive therapy	4 (23%)	1 (6%)	3 (17%)	**<0.05***
Corticosteroid usage	2 (11%)	0	2 (11%)	**<0.05***
Concomitant bacteremia	1 (6%)	0	1 (6%)	0.19
Coinfection with TB	0	0	0	0.44
Misdiagnosed with TB	1 (6%)	1 (6%)	0	0.35
Sepsis	1 (6%)	0	1 (6%)	0.19

*P-value is significant (p<0.05)

Compared to combined therapy, single medication therapy was used more often (5/18; 28%) than combination therapy (4/18; 23%). In the case of single-drug therapy, namely minocycline, there was a statistically significant difference in antibiotic treatment and treatment duration between the two groups (lung and disseminated) (p0.05). The TMP-SMX therapy came close to the threshold for significance (p=0.07). Similarly, the difference in antibiotic treatment and treatment duration between the Lung and Disseminated groups was substantial when combination therapy was used (table 3). Participants with both pulmonary and disseminated nocardiosis were more probable to have have fundamental illnesses including cancer or chronic pulmonary disease in addition to N. asteroides illnesses. These patients also came with clinically urgent circumstances, such as sepsis, and were frequently incorrectly diagnosed with TB at first. In addition, the patients often received immunosuppressive medication and combination antibacterial therapy.

Table3. Antibiotics treatment and Duration of treatment days

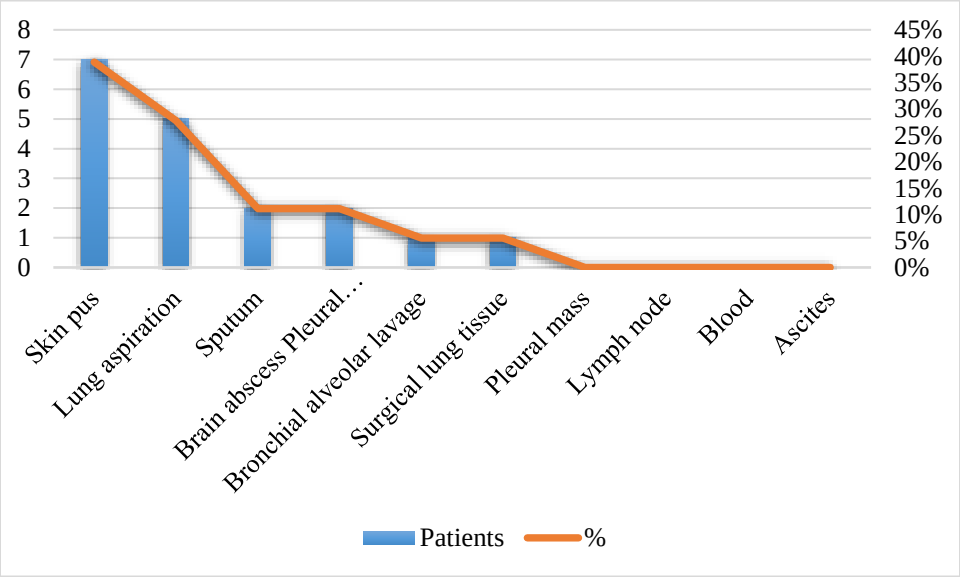
Variable	Total	Lung	Disseminated	P-value
	n (%)	n (%)	n (%)	
Single drug therapy	5 (28%)	3 (17%)	2 (11%)	**0.03***

TMP-SMX	3 (17%)	3 (17%)	0	0.07
Penicillin or cephalosporin	1 (6%)	1 (6%)	0	0.21
Minocycline	0	0	0	**<0.01***
Combinedtherapy	4 (23%)	1 (6%)	3 (17%)	**0.01***
Notherapy	2 (12%)	1 (6%)	1 (6%)	0.36
Treatmentinadequacy	3 (17%)	2 (11%)	1 (6%)	0.61

*P-value is significant ($p<0.05$)

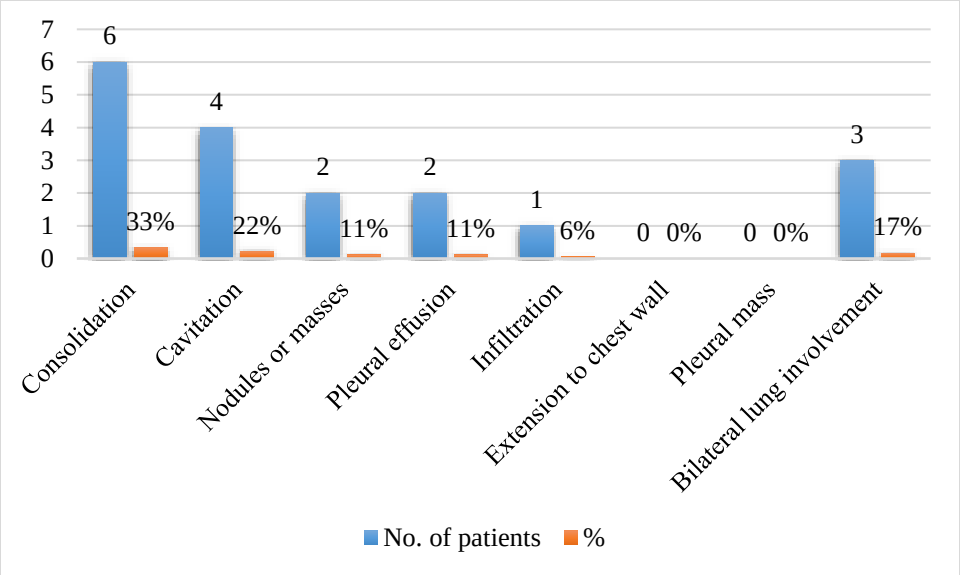
Figure 2 demonstrates that Nocardia was obtained and cultivated from a wide variety of sources. The cultures of skin pus was necessary for the identification of lung nocardiosis(n=7; 39%), lung aspiration (n= 5; 28%), sputum (n=2; 11%), brain abscess pleural effusion (n=2; 11%), bronchial alveolar lavage (n=1; 6%), and surgical lung tissue (n=1; 6%).

Figure2. Diagnosticmethodsofcultured-provennocardiosis.



The x-ray findings of 18 individuals with nocardiosis involving the lungs are shown in Figure 3. (including disseminated type with lung involvement). There were six cases of consolidation (33%), four cases of cavitation (22%), three cases of bilateral lung involvement (17%), two cases of nodules or masses (11%), one case of pleural effusion (6%), and one case of infiltration (6%).

Figure 3. Chest radiography observations showing nocardiosis involving the lungs (both disseminated nocardiosis and localized lung).



Infectious areas across the body are shown in Table 4 together with the antimicrobial susceptibilities of the corresponding Nocardia species. More over a third (six of eighteen, or 33%) of the isolates were sensitive to Amikacin, whereas a similar percentage were resistant to TMP/SMZ. These tests revealed that the susceptibility of extract viapulmonary and disseminated diseases to Minocycline (3/18; 17%), Cefotaxime (1/18; 6%), Gentamicin (1/18; 6%), and Ampicillin (1/18; 6%) was considerably lower.

Table4. Evaluation of Nocardia species recovered from individuals with various disease locations for their antibacterial sensitivity

Antibiotic tested	Lung		Disseminated		Total		p
	n	%	n	%	n	%	
Amikacin	4	22%	2	11%	6	33%	0.07
TMP/SMZ	4	22%	2	11%	6	33%	0.13
Minocycline	2	11%	1	6%	3	17%	0.38
Cefotaxime	1	6%	0	0%	1	6%	0.23
Gentamicin	1	6%	0	0%	1	6%	**<0.01***
Ampicillin	0	0%	1	6%	1	6%	0.81
Total	12	67%	6	33%	18	100%	

*P-value is significant ($p<0.05$)

Discussion

Based on the outcomes of our study, those with chronic pulmonary disease, cancer, diabetes, autoimmune disorders, and HIV infection, and are receivers of organ transplants are more likely to get an infection caused by Nocardia. In spite of the fact that a number of articles detailing the clinical and microbiologic characteristics of nocardiosis have been published, disseminated nocardiosis is only seldom documented (Tuo et al., 2008, Liu et al., 2011; Lai et al., 2011). According to this report, patients who had disseminated and lungs nocardiosis were more likely to havemalignancy, chronic lung disease and concomitant bacteremia, were frequently given the wrong diagnosis of tuberculosis, were receiving immunosuppressive treatments, and had a higher mortality rate than those who had skin infections. We have also shown that Nocardia strains that are isolated from individuals who have lung infections or

illnesses that have spread throughout the bodycompared to those produced from skin problems, to be less resistant to antimicrobials in vitro.These results are consistent with those that were discovered by Wang et al (2015).

N. asteroids is responsible for 60–80% of all cases in Western nations, but N. brasiliensis is seldom seen in these regions. In point of fact, N. brasiliensis is discovered in temperate regions only very seldom. However, it has been isolated from the ground in a great number of tropical and subtropical nations (Farina et al., 1995; Brown-Elliott et al., 2006; Pintado et al., 2002). It has been found that N. brasiliensis is most often connected with diseases that affect the skin. The patient in our cohort who developed mycetoma on a lower leg had been suffering from persistent ulcers for more than a decade. The doctor had incorrectly classified the lesions as an infection caused by Actinomycetes due to the presence of sulfa granules in the pathological results. Following the discovery of Nocardia, this patient was able to obtain the treatment that was most suited for their condition. Culture analysis is required in order to get an accurate diagnosis. The overall percentage of cases with nocardiosis in this group that did not have an underlying illness was 45%. Everyone who had been diagnosed with skin nocardiosis had made a full recovery.

There is a paucity of data pertaining to the relationship between impaired immune function and the progression of nocardiosis. TMP/SMX, an anti-Nocardia medication, is given to a significant number of HIV-positive patients and transplant recipients who have been diagnosed with nocardiosis. This is done either for the prevention or treatment of pneumocystis jiroveci infections, which are frequent in both patient groups. The percentage of HIV-positive individuals in this group who were resistant to TMP/SMX was 25%. Patients who have tested positive for HIV, and are also infected with Nocardia species will be of significant interest to researchers conducting investigations in the future.

In this investigation, 33 percent of patients demonstrated TMP/SMX susceptibility; nevertheless, in some places, more than 50 percent of Nocardial strains are resilient to this treatment (Mootsikapun et al., 2005). The showing of in vitro vulnerability is not necessarily proportional to clinical efficacy (Munoz et al., 2007), despite the fact that in vitro studies indicated that 33 percent of our isolates were susceptible to amikacin. Participants in this subgroup who had pulmonary or disseminated infections had a higher likelihood of having resistance Nocardia strains found in their bodies. The primary therapeutic plans for individuals on immunosuppressive medications who have lung, disseminated, or cerebral nocardiosisare combined with imipenem, third-generation cephalosporins, or minocycline alongside or without amikacin (Ambrosioni et al., 2010). It has been proposed that patients who have lung or disseminated nocardiosis need combination therapy as an empirical therapy prior to antimicrobial susceptibility testing. Patients who require this kind of medication also have a higher demand for treatment.

Conclusion

A mean age of 57.8 years was observed across all of the patients, the majority of whom were male. Although N. asteroides was mostly responsible for the overall incidence (44%) of the disease, N. brasiliensis was primarily responsible for the bulk of the disseminated cases that occurred (22%). Chronic pulmonary illness was the most frequent underlying condition, accounting for 17% of cases, followed by cancer, which accounted for 12%. The use of a single medicine was the method of treatment that occurred the most often (28%). Patients who suffered from lung and disseminated nocardiosis, on the other hand, were more likely to have infections caused by N. asteroides and an underlying illness, such as chronic lung disease or cancer. These individuals also came with clinically urgent circumstances, such as sepsis, and were often originally diagnosed with TB when they really did not have the disease. In addition to this, immunosuppressive medication and combination antibiotic therapy were often administered to the patients. It has been proposed that patients who have lung or disseminated nocardiosis need combination therapy as an empirical therapy prior to antimicrobial susceptibility testing.

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