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ORIGINAL RESEARCH

Species Distribution And Antibiotic Susceptibility Of *Nocardia* Isolates From Yantai, China

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Purpose: This study aimed to investigate the species distributions and drug sensitivities among 19 strains of *Nocardia* isolated from Yantai, China, from 2017 to 2019.

Patients and methods: Definitive species identification was performed by sequencing a fragment of the 16S rRNA gene (1480 bp) and by matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF MS). The susceptibilities of the isolates to 15 commonly-used antibiotics were tested using the microbroth dilution method.

Results: Among the 19 *Nocardia* isolates, five species were confirmed. Seventeen of the 19 *Nocardia spp*. strains were identified consistently by the two methods, while two isolates of *N. cyriacigeorgica* were misidentified as *N. otitidiscaviarum* by MALDI-TOF MS. *N. farcinica* was the most common species (8/19), followed by *N. cyriacigeorgica* (6/19), *N. otitidiscaviarum* (2/19), *N. brasiliensis* (2/19), and N. *nova* (1/19). All isolates were susceptible to trimethoprim-sulfamethoxazole and amikacin, followed by linezolid and tigecycline (94.7% susceptibility rates). The sensitivity and minimum inhibitory concentration patterns for ciprofloxacin, moxifloxacin, clarithromycin, and tobramycin were significantly correlated with the species.

Conclusion: These results regarding the distribution and antibiotic resistance features of *Nocardia* species further our understanding of the diversity of *Nocardia* species circulating in Yantai, China, and thus support the use of more accurate empirical treatments.

Keywords: antibiotic susceptibility, *Nocardia*, nocardiosis, species distribution

Introduction

Nocardia comprises a genus of naturally occurring bacteria that can be isolated from water, soil, dust, decaying vegetation, and animal waste, and which can be responsible for opportunistic infections in immunocompromised and immunocompetent patients.[1] *Nocardia* infection can lead to pneumonia, brain abscesses, and skin and soft tissue infections.[2] Nocardiosis has been increasingly reported in recent years worldwide,[3–5] though the distribution and antibiotic susceptibility of *Nocardia* varies geographically and over time.[6,7] *Nocardia* is traditionally identified by biochemical methods, but the success rate is low. Data on the distribution of *Nocardia* species and the associated drug susceptibility patterns in Yantai, China, are thus currently lacking.[8] To the best of our knowledge, the present study provides the first comprehensive evaluation of the clinical features, species identification, distribution, and antibiotic susceptibility profiles of *Nocardia* in a coastal city in China.

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Materials And Methods

Strain Collection

Nineteen non-repetitive strains of *Nocardia* were collected from clinical specimens from seven hospitals in Yantai, Shandong Province, China, from January 2017 to March 2019. Of these, 13 were from Yantai Yuhuangding Hospital, which is the Regional Medical Center in Yantai, and the other six strains were isolated from six different central hospitals in Yantai city. Nineteen isolates from clinical specimens including sputum, bronchoalveolar lavage fluid, puncture fluid (knee-joint, hepatophyma liver abscess, pleural effusion), and skin and soft tissue pus were inoculated onto Columbia blood agar plates and cultured. All the strains were forwarded to Yantai Yuhuangding Hospital. Approval by the institutional review board and informed consent was obtained for experimentation with human subjects. Definitive identification was performed by microbial matrix-assisted laser desorption/ionization-time of flight (MALDI-TOF) mass spectrometry (Microflex MALDI Biotyper; Bruker, Madison, WI, USA) and sequencing of a fragment of 16S rRNA gene.

Mass Spectrometry

For the standard Bruker MALDI-TOF MS preparation procedure, samples were collected from the plate and re-suspended in 300 µl sterile water. Absolute ethanol (900 µl) was added, the tubes were vortexed briefly and then centrifuged 13,000 rpm for 2 mins. The supernatant was removed, and the pellets were dried at room temperature. Then 70% formic acid (20 µl) and acetonitrile (20 µl) was added to each pellet. Samples were vortexed and centrifuged 13,000 rpm for 2 mins, 1 µl of the supernatant was placed on a MALDI target plate and allowed to air dry. After drying, spots were overlaid with 1 µl matrix solution and again allowed to dry. Mass spectrometry was performed on a MALDI Biotyper 3.1 Microflex LT system using the manufacturer's settings. Species-level identification was accepted if the score was ≥ 2.00; genus-level identification was accepted if the score was 1.70–2.00.

DNA Extraction, PCR, And Sequencing

DNA was extracted from *Nocardia* strains using a TIANGEN Genomic DNA kit (TIANGEN Biotech, Beijing, China) according to the manufacturer's instructions. In brief, isolated colonies were mixed with 400µl NF-H_2O in a microcentrifuge tube. Then 3 µl RNase A was added to the tube and mixed by pulse vortexing for 5 mins. The column was centrifuged at 15,000 g for 2 mins. The supernatant was added with 400 µl buffer GP2 and the whole mixture was transferred to a mini spin column. The column was centrifuged at 12,000 rpm for 30 seconds, and the filtrate was discarded. After sequential washes with 600 µl buffer GD, 700 µl buffer PW, DNA was eluted with 20 µl NF-H_2O and stored at −20°C.

The isolated *Nocardia* strains were identified at the species level by sequencing of the 16S rRNA gene (1480 bp) as described previously.[9] PCR amplification and sequencing of the 16S rRNA gene were performed with the universal primers 27F (5′-AGAGTTTGATCCTGGCTCAG-3′) and 1492R (5′-GGTTACCTTGTTACGACTT-3′). The polymerase chain reaction (PCR) products were purified and sequenced by a genetic testing laboratory (Zhejiang Tianke High-tech Development Co., Ltd., Hangzhou, Zhejiang, China). PCR reactions were conducted using 96-well plates with a total reaction volume of 25 µl per well containing 12.5 µl phanta Max Master Mix (Vazyme, Nanjing, China), 0.5 µl each primer, 2.5 µl DNA, and 9 µl RNase-free water. The thermal cycling conditions of PCR were as follows: 95 °C for 2 mins, followed by 30 cycles of 95 °C for 30 s, 55°C for 30s and 72 °C for 30 s. Identification of *Nocardia* isolates at the species level species was based on a similarity value of ≥99.0% as described previously.[9,10] *Nocardia* species determined by the 16S rRNA gene at NCBI GenBank using BLAST software (http://www.ncbi.nlm.nih.gov) and leBIBI database (https://umr5558-bibiserv.univ-lyon1.fr/lebibi/lebibi.cgi).

Antibiotic Susceptibility Testing

Antibiotic susceptibility testing was performed using the microbroth dilution method (Sensititre Susceptibility plates; TREK Diagnostic Systems Ltd., Cleveland, OH, USA). The antibiotics tested were amikacin, trimethoprim-sulfamethoxazole (SXT), moxifloxacin, ciprofloxacin, cefepime, imipenem, ceftriaxone, amoxicillin-clavulanate, linezolid, doxycycline, cefoxitin, minocyline, tigecycline, tobramycin, and clarithromycin. The minimum inhibitory concentration (MIC) breakpoints were interpreted following the CLSI recommendations M24-A for aerobic actinomycetes.[11] Briefly, colonies of identified isolates growing on blood agar were collected and transferred into sterile 0.85% sodium chloride solution and vortexed repeatedly. The supernatant was then adjusted to a turbidity of 0.5 McFarland, 50 µl bacterial suspension was spread into Sensititre® cation-adjusted Mueller–Hinton broth with TES (TREK Diagnostic Systems) and the MICs were determined according to the instructions for the Sensititre Susceptibility plates after 72 h of incubation at 35°C. *Staphylococcus aureus*

ATCC 29213 and *Escherichia coli* ATCC 35218 were used as controls.

Results

Distribution Of *Nocardia* Species

Five species were confirmed among the 19 *Nocardia* isolates. The clinical features are shown in Table 1. *N. farcinica* was the most common species (42.1%, 8/19), followed by *N. cyriacigeorgica* (31.6%, 6/19), *N. otitidiscaviarum* (10.5%, 2/19), *N. brasiliensis* (10.5%, 2/19), and *N. nova* (5.3%, 1/19), respectively. Two samples of *N. cyriacigeorgica* were misidentified as *N. otitidiscaviarum* by the MALDI Biotyper. In addition to gene sequencing analysis, phylogenetic relationships based on the 16S rRNA gene were also used to identify the 19 clinical *Nocardia* isolates (Figure 1).

According to the criteria for judging invasive and non-invasive cases, six (24.5%) *Nocardia* strains isolated from sterile sites were considered to be non-invasive and the other 13 (75.5%) isolated from sputum, bronchoalveolar lavage fluid, and skin and soft tissue were considered to be non-invasive. Invasive cases included *N. farcinica* (3/6) isolated from joint infections (2/3) and hepatapostema (1/3), and *N. cyriacigeorgica* (3/6) isolated from whole blood (2/3) and pleural effusion (1/3).

Patient Characteristics

The individual characteristics of the 19 patients are shown in Table 1. The isolates were distributed evenly throughout the study period and no outbreaks were detected. Nocardiosis was diagnosed in 15 (78.9%) men and four (21.1%) women (age range 27–82 years, mean 57.2±17.3). No strains were isolated from children, even though one hospital included a 300-bed pediatric ward.

Underlying Diseases

Fifteen patients (78.9%) had underlying diseases (independent or simultaneous), including diabetes mellitus (n=9), pulmonary lesions (n=4), nephrotic syndrome (n=3), autoimmune disease (n=2), malignant tumor (n=2), and hematologic disease (n=1). The other five patients were immunocompetent, but one had pneumonia and four had arthritis and local infection.

Antibiotic Susceptibility Profiles

The susceptibilities of the *Nocardia* isolates to the 15 antibiotics are summarized in Table 2. *Nocardia* was most sensitive to SXT, linezolid, amikacin, and tigecycline, with sensitivities of 100%, 100%, 94.7%, and 94.7%, respectively. However, the sensitivities to imipenem and moxifloxacin were only 31.5% and 47.3%, and to ceftriaxone, amoxicillin-clavulanic acid, cefepime, oxycycline, minocycline, and clarithromycin were 21%, 10.5%, 10.5%, 5.26%, 5.26%, and 5.26%, respectively.

Correlations Between Antimicrobial Susceptibility Profiles And *Nocardia* Species Designations

The correlations between drug susceptibility patterns and *Nocardia* species are demonstrated in Table 3. Susceptibility patterns *per se* were not indicative of a particular species, but *N. farcinica*, N. *cyriacigeorgica*, and *N. nova* all had certain characteristics not seen in *N. brasiliensis* and *N. otitidiscaviarium*.

Discussion

Only a few species of *Nocardia*, including *N. brasiliensis*, N. *farcinica*, and *N. pseudobrasiliensis*, can currently be reliably identified using traditional biochemical methods.[12] Although molecular biology techniques (16S rRNA gene PCR and sequencing) allow more species within the *Nocardia* genus to be described,[8] molecular identification techniques are difficult to carry out routinely in China because of high cost and a lack of standardization. However, MALDI-TOF MS technology has recently made the identification of bacteria faster and more convenient. In the current study, we used both methods to identify the 19 isolated strains of *Nocardia*, and showed that the results of the two methods were consistent for *N. farcinica*, N. *brasiliensis*, N. *otitidiscaviarium*, and *N. nova*, but that two strains of *N. cyriacigeorgica* were misidentified as *N. otitidiscaviarium*. These results suggested that, although MALDI-TOF MS was accurate for the genus-level identification of *Nocardia*, it could not reliably distinguish among *Nocardia* species.

More than 50 species of *Nocardia* have been identified as human pathogens to date,[12] including species distributed in various geographic regions.[13] The five species found in the current study were the most prevalent in different parts of the world.[12] However, it was interesting to note that *N. otitidiscaviarum* and *N. brasiliensis* isolates, which are commonly found in tropical countries,[14] were also isolated from samples from our temperate region. This may be associated with increases in world population mobility, but homology analysis is needed to explain this

Table 1 Clinical Features Of 19 *Nocardia* Isolates

Strain No.	Species By MALDI Biotyper	Species By16SrRNA	Accession Number	Age	Gender	Specimen	Clinical Diagnosis Underlying Diseases	Concurrent Infection	Initial Empirical Medication	Adjust Medication After Identifying Pathogen	Outcome
A3615	*N. farcinica*	*N. farcinica*	NR_117248.1	71	Female	Sputum	Pneumonia/ bronchiectasis/ endometrial cancer	No	BIA+LZD	SXT+IPM	recovered
A2671	*N. farcinica*	*N. farcinica*	NR_117248.1	58	Male	Sputum	Pneumonia/diabetes mellitus/nephrotic syndrome	No	AMX+AZM	SXT	recovered
A0495	*N. farcinica*	*N. farcinica*	NR_117248.1	82	Male	Sputum	Pneumonia/diabetes mellitus	No	MXF+IPM	SXT	recovered
A2788	*N. farcinica*	*N. farcinica*	NR_117248.1	29	Male	Drainage,	SSTIS/no	No	Cephalosporins (NA)+LEV	SXT+AMC	recovered
A2754	*N. farcinica*	*N. farcinica*	NR_117248.1	37	Male	Drainage,	Joint infection/no	No	Cephalosporins (NA)	SXT+LZD	recovered
A0457	*N. farcinica*	*N. farcinica*	NR_117248.1	36	Male	Drainage	SSTIS/no	No	Cephalosporins (NA)	SXT	Recovered
A2850	*N. farcinica*	*N. farcinica*	NR_117248.1	54	Female	Puncture fluid	Hepatapostema/ Nephrotic syndrome/ Diabetes mellitus	No	TZP+VCZ	SXT+IPM+LZD	Recovered
A2849	*N. farcinica*	*N. farcinica*	NR_117248.1	77	Male	Synovial Fluid	Joint infection/no	No	NA	SXT	Recovered
A3092	*N. brasiliensis*	*N. brasiliensis*	NR_117247.1	78	Male	Pus	SSTIS/diabetes mellitus	No	TZP	SXT	Recovered
A2748	*N. brasiliensis*	*N. brasiliensis*	NR_117247.1	54	Male	Pus	SSTIS/diabetes mellitus	No	TZP	SXT	Recovered
A2229	*N. otitidiscaviarium*	*N. otitidiscaviarium*	NR_117344.1	55	Female	BALF	Pneumonia/COPD	No	TZP+LEV	SXT+DOX	Recovered
A2350	*N. otitidiscaviarium*	*N. otitidiscaviarium*	NR_117344.1	58	Male	Sputum	Pneumonia/diabetes mellitus	No	TZP	SXT	Recovered
A3594	*N. nova*	*N. nova*	NR_117343.1	72	Female	Sputum	pneumonia/diabetes mellitus/siccasyndrome	Aspergillus	TZP	SXT+IPM	Death
A1175	*N. otitidiscaviarium*	*N. cyriacigeorgica*	NR_117334.1	41	Male	Sputum	pneumonia		TZP+LEV	SXT	Recovered

A2525	N. cyriacigeorgica	N. cyriacigeorgica	NR_117334.1	68	Male	Whole Blood	pulmonary abscess/ septicemia nephrotic syndrome		TZP	SXT+LZD	Recovered
A2427	*N. otitidiscaviarium*	*N. cyriacigeorgica*	NR_117334.1	27	Male	Pleural Effusion	pneumonia/myasthenia gravis/thymic carcinoma	Aspergillus	AZM+ VCZ +LZD	IPM+SXT+LZD+VRC	Death
A3603	*N. otitidiscaviarium*	*N. cyriacigeorgica*	NR_117334.1	65	Male	Sputum	Pneumonia/diabetes mellitus/COPD	Aspergillus	TZP+LEV+SCF	MXF+MEM+VRC	Recovered
A0494	*N. cyriacigeorgica*	*N. cyriacigeorgica*	NR_117334.1	60	Male	BALF	Pneumonia/ bronchiectasis		MXF	SXT+BIA+AZM	Recovered
A2483	*N. cyriacigeorgica*	*N. cyriacigeorgica*	NR_117334.1	66	Male	Whole Blood	Pneumonia/AML/ diabetes mellitus		IPM+TEC	MXF+TEC	Death

Abbreviations: NA, not available; AMK, amikacin; AMC, amoxicillin-clavulanic acid; FEP, cefepime; CRO, ceftriaxone; CIP, ciprofloxacin CLR, clarithromycin; DOX, doxycycline; IPM, imipenem; LZD,linezolid; MIN, minocycline; MXF, moxifloxacin; TOB, tobramycin; SXT, trimethoprim-sulfamethoxazole; BIA, biapenem; AMX, amoxicillin; AZM, azithromycin; LEV, levofloxacin; TZP, piperacillin-tazobactam; VCZ, voriconazole.

issue. Moreover, *N. farcinica* was the predominant species in our area, which differed from the patterns in the United States,[7] Taiwan,[15] Spain,[16] and Iran,[17] where *N. nova*, N. *brasiliensis*, and *N. asteroides* were the most prevalent species, respectively. *N. brasiliensis* is associated with insect bites all over the world so this could be another fact.

Fourteen of the 19 patients in the current study had at least one significant underlying condition. The types of underlying diseases were similar to those reported by Hashemi-Shahraki et al.[17] although the proportions were slightly different. The most frequent conditions were diabetes mellitus (9 patients, 64.2%), followed by chronic lung disease (chronic obstructive lung disease or bronchiectasis; four patients, 28.5%), nephrotic syndrome (three patients, 21.4%), cancer (two solid tumors patients and one hematologic malignancy, 10.8%), and autoimmune diseases (two patients, 14.3%), while four (80%) of five patients with skin and soft tissue and joint infections had no underlying conditions.

Sulfamethoxazole and Trimethoprim (SXT), linezolid, and imipenem are the usual drugs for the empirical treatment of nocardiosis.[18] However, only five of the 19 patients (26%) received initial empirical medication with one or both combinations, indicating the need to identify the infectious pathogens. After the pathogen was identified, 17 of the 19 patients received SXT alone or combined with other drugs, while the other two patients received moxifloxacin combined with other drugs. Each patient changed from empirical to targeted treatment, and 16 of the 19 patients achieved good therapeutic effects and were discharged after improvement. Three patients died, including two who were also infected with *Aspergillus* and one with a bloodstream *Nocardia* infection, suggesting that coexisting *Aspergillus* and bloodstream infections may be risk factors for a poor prognosis in patients with *Nocardia* infections.

The CLSI guidelines recommend broth microdilution for determining the antimicrobial susceptibility of *Nocardia* spp.[11] and McTaggart et al.[2] demonstrated the suitability of the Sensititre Rapmyco microdilution panel for the determination of antimicrobial susceptibility patterns in clinical isolates of *Nocardia* spp. As in other studies,[2,5] five species showed good sensitivity to amikacin, linezolid, and SXT with MIC90 values of 1, 2, and 0.25 μg/mL, respectively, and susceptibility and sensitivity rates of 100% for all isolates. However, other studies[5,8] reported higher resistance to SXT among *N. farcinica*, but low rates of SXT treatment failure. This apparent

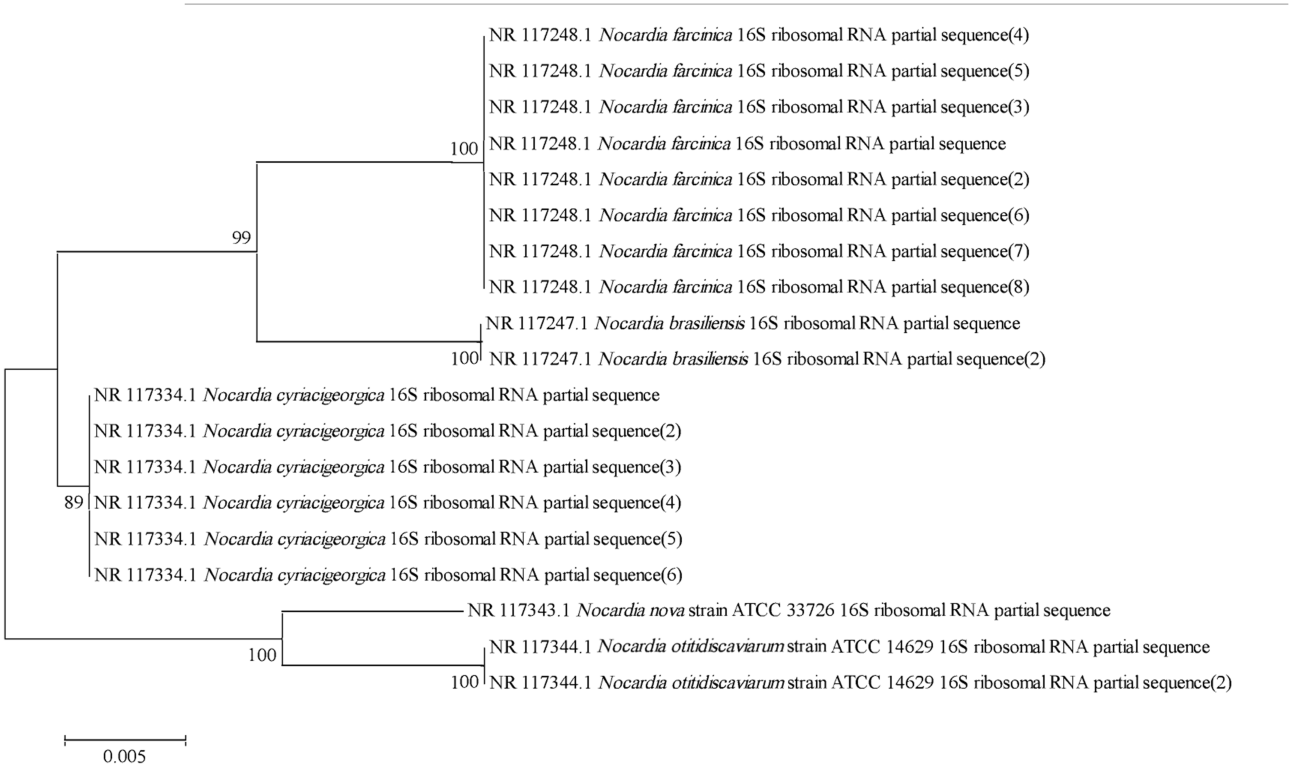

Figure 1 16S rRNA sequence-based phylogenetic tree of clinical isolates of *Nocardia* with those of closely related species which computed by the NJ analyses.

discrepancy may indicate a defect in the method of drug sensitivity testing, or differences between the results of drug sensitivity tests in vitro and drug action in vivo. Imipenem is one of the recommended empirical drugs,[18] but the present study found that only 31.5% of isolates were sensitive to imipenem, with drug-resistant or moderately drug-resistant strains distributed among the other four species, suggesting that imipenem is no longer suitable for clinical treatment of *Nocardia* infection. The sensitivities to the three tetracycline drugs were similar to a previous report,[19] with sensitivities to minocycline and doxycycline of 5.26% but MIC values indicating moderate drug resistance, while the sensitivity to tigecycline was 94.7% and the MIC90 was 1 μg/mL, suggesting that tigecycline might be a useful empirical clinical treatment. The sensitivity rates to cephalosporins and amoxicillin-clavulanic were 21% or less, with slight differences among the strains. Only *N. cyriacigeorgica* had a sensitivity rate of 50% to ceftriaxone.

We found a correlation between the drug susceptibility patterns and species in relation to ciprofloxacin, moxifloxacin, clarithromycin, and tobramycin, in line with previous reports of links between *Nocardia* taxonomy and specific patterns of antimicrobial susceptibility.[2] In the present study, no isolates of *N. farcinica* were ciprofloxacin-resistant, while the other four species were all ciprofloxacin-resistant. Two N. *otitidiscaviarum* isolates were resistant to ciprofloxacin as reported by McTaggart et al.[2] but in contrast to Brown-Elliott et al.[12] who indicated that they were susceptible to ciprofloxacin. The MIC values of ciprofloxacin and moxifloxacin in *N. farcinica* were similar, but significantly different from other strains. The N. *nova* was sensitive to clarithromycin with a MIC value ≤0.06, in sharp contrast to the other four species. There were obvious differences in tobramycin sensitivity between *N. farcinica* and *N. nova* and the other three species. Interestingly, the two *N. cyriacigeorgica* strains wrongly identified by mass spectrometry could be distinguished by their MIC values, given that the MIC values of *N. cyriacigeorgica* isolates to tobramycin were all ≤1, while *N. otitidiscaviarum* was sensitive, but had a high MIC value.

Although the number of strains in our experiment was limited, the antibiotic susceptibility patterns *per se* were not indicative of a particular species. However, the results suggested that *Nocardia* isolates identified on the basis of other phenotypic characteristics but with conflicting susceptibility test results should be further examined and confirmed.

Table 2 Antimicrobial Susceptibility, MIC50 And MIC90 Of 19 *Nocardia* Isolates

Species	SXT	LZD	CIP	MXF	AMC	CRO	FEP	FOX	IPM	TOB	AMK	DOX	MIN	TGC	CLA
Susceptible %	100	94.7	36.8	47.3	10.5	21	10.5	5.26	31.5	52.6	100	5.26	5.26	94.7	5.26
MIC 50	0.25	2	≥8	1	16	≥128	≥64	128	8	2	≤1	4	4	0.5	≥32
MIC 90	0.25	2	≥8	4	32	≥128	≥64	≥128	≥128	16	≤1	4	4	1	≥32
N. farcinica	≤0.25	2	**2**	**2**	16	≥128	≥64	64	8	16	≤1	4	2	2	≥32
N. farcinica	≤0.25	2	**0.25**	**≤0.25**	16	≥128	≥64	≥128	8	16	≤1	4	4	1	≥32
N. farcinica	≤0.25	2	**1**	**≤0.25**	16	≥128	≥64	≥128	32	16	≤1	4	4	1	≥32
N. farcinica	≤0.25	≤1	**0.5**	**≤0.25**	16	≥128	≥64	128	16	16	≤1	4	4	0.5	≥32
N. farcinica	≤0.25	≤1	**0.5**	**≤0.25**	16	≥128	≥64	≥128	16	≥32	≤1	4	2	0.5	≥32
N. farcinica	≤0.25	2	**0.5**	**≤0.25**	8	≥128	≥64	64	8	16	≤1	4	4	0.5	≥32
N. farcinica	≤0.25	2	**0.25**	**≤0.25**	16	≥128	≥64	128	16	16	≤1	4	2	0.5	≥32
N. farcinica	≤0.25	2	**1**	**≤0.25**	8	16	32	32	4	8	≤1	4	2	1	≥32
N. brasiliensis	0.5	4	≥8	2	16	≥128	≥64	≥128	≥128	**≤1**	≤1	4	2	0.5	≥32
N. brasiliensis	≤0.25	2	≥8	1	16	≥128	≥64	≥128	≥128	**≤1**	≤1	4	2	0.5	≥32
N. cyriacigeorgica	≤0.25	16	≥8	8	32	8	16	128	8	**≤1**	2	4	4	1	≥32
N. cyriacigeorgica	≤0.25	≤1	≥8	4	16	4	4	128	≤2	**≤1**	≤1	2	4	1	≥32
N. cyriacigeorgica	≤0.25	2	≥8	2	32	16	≥64	128	8	**≤1**	≤1	8	4	1	≥32
N. cyriacigeorgica	≤0.25	2	≥8	4	32	4	16	128	4	**≤1**	≤1	4	4	1	≥32
N. cyriacigeorgica	≤0.25	≤1	≥8	2	32	≥128	≥64	128	≤2	**≤1**	≤1	2	2	1	≥32
N. cyriacigeorgica	≤0.25	2	≥8	4	32	16	≥64	128	4	**≤1**	≤1	4	4	1	≥32
N. otitidiscaviarium	≤0.25	2	≥8	1	32	≥128	≥64	≥128	64	4	≤1	1	4	0.25	≥32
N. otitidiscaviarium	≤0.25	≤1	≥8	4	≥128	≥128	≥64	≥128	≥128	2	≤1	2	≤1	0.5	≥32
N. nova	≤0.25	≤1	≥8	4	≥128	8	8	16	≤2	≥32	≤1	16	4	0.5	**≤0.06**

Abbreviations: AMK, amikacin; AMC, amoxicillin-clavulanic acid; FEP, cefepime; CRO, ceftriaxone; CIP, ciprofloxacin; CLR, clarithromycin; DOX, doxycycline; IPM, imipenem; LZD,linezolid; MIN, minocycline; MXF, moxifloxacin; TOB, tobramycin; SXT, trimethoprim-sulfamethoxazole.

Table 3 Antimicrobial Susceptibility Patterns Of Different *Nocardia* Species

Nocardia Species	No Of Isolates	Drug Patterns Types	Antimicrobial Susceptibility Pattern			
			non-Susceptible(Intermediate And Resistant)(%)		Susceptible(%)	
N. farcinica	8	V	CRO FEP TOB CLA	100 100 100 100	SXT AMK LZD TGC MXF CIP	100 100 100 87.5 87.5 87.5
N. cyriacigeorgica	6	VI	CIP CLA AMC	100 100 100	SXT AMK TGC TOB LZD	100 100 100 100 83
N. brasiliensis	2	VIII	CIP CLA CRO FEP IPMc	100 100 100 100 100	SXT AMK TGC LZD TOB	100 100 100 100 100
N. otitidiscaviarium	2	VII	CIP CLA CRO FEP IPMc	100 100 100 100 100	SXT AMK TGC LZD TOB	100 100 100 100 100
N. nova	1	III	CIP AMC TOB DOX	Ra	CLA CRO FEP	Sa

Abbreviations: a, only one stain; AMK, amikacin; AMC, amoxicillin-clavulanic acid; FEP, cefepime; CRO, ceftriaxone; CIP, ciprofloxacin; CLR, clarithromycin; DOX, doxycycline; IPM, imipenem; LZD,linezolid; MIN, minocycline; MXF, moxifloxacin; TOB, tobramycin; SXT, trimethoprim-sulfamethoxazole.

Conclusion

In conclusion, the present retrospective study reports 19 nonrepetitivce clinical *Nocardia* strains isolated and characterized from Yantai, China, in terms of their species, distribution, and antibiotic profiles. These results will improve our understanding of the clinical features of nocardiosis and of the *Nocardia* species distributed in our area, and will thus aid decision-making in the context of empirical treatment.

Disclosure

The authors report no conflicts of interest in this work.

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