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SUSCEPTIBILITY

Retrospective Analysis of Antimicrobial Susceptibility Profiles of *Nocardia* Species from a Tertiary Hospital and Reference Laboratory, 2011 to 2017

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ABSTRACT *Nocardia* species are found worldwide and are opportunistic pathogens of both immunocompromised and immunocompetent hosts. Recent updates to the taxonomy of this genus have indicated that there are more than 90 recognized species of *Nocardia* with 54 species reported to be clinically relevant. In this paper, we report the species distribution, specimen source distribution, and antimicrobial susceptibility profiles of 2,091 clinical isolates recovered for the years 2011 to 2017 using the updated taxonomy. The most commonly isolated species included *Nocardia nova* complex, *Nocardia cyriacigeorgica*, and *Nocardia farcinica* complex, with an additional 25 species or species complexes recovered from clinical specimens. The antimicrobial susceptibility profile was highly variable between the species, but in general, amikacin, linezolid, and trimethoprim-sulfamethoxazole demonstrated good *in vitro* activity against most species.

KEYWORDS *Nocardia*, antimicrobial agents, epidemiology

Nocardia species are found throughout the world in water, soil, and other organic matter. Although these are generally considered opportunistic pathogens that cause disease in immunocompromised patients, approximately one-third of cases involve immunocompetent hosts (1, 2).

The data available on the incidence of nocardiosis are limited, but it is estimated that there are 500 to 1,000 new cases annually in the United States (3). *Nocardia* is usually acquired through inhalation of the organism, but traumatic inoculation into the skin also occurs, and the organism has been reported to be nosocomially acquired through direct inoculation of the skin by contaminated catheters or surgical equipment. *Nocardia* infections are not thought to be transmitted from person to person (4, 5).

Nocardia species can cause a wide variety of clinical syndromes, with pulmonary infections being the most common manifestation. *Nocardia* species are also responsible for extrapulmonary infections with a predilection for the central nervous system, skin, and subcutaneous tissue. *Nocardia* bacteremia is extremely rare, even in an immunocompromised population (6).

Since first being identified in 1889, *Nocardia* taxonomy has been challenging and has continued to evolve, with more than 90 currently recognized species (7). Differences in susceptibility profiles, clinical presentation, and treatment options necessitate the identification of *Nocardia* to species level in order to provide optimal patient care.

In the laboratory, *Nocardia* species are slow-growing, aerobic, weakly acid-fast, Gram-positive, branching bacteria that are classically described as having a beaded appearance on Gram stain. Phenotypic and biochemical identification methods are not able to sufficiently discriminate between the species, so currently, matrix-assisted laser desorp-

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TABLE 1 Characteristics of 2,091 *Nocardia* isolates from 2011 to 2016

Characteristic	No. (%)
Patient demographics	
Median age (range) (yrs)	66 (55–76)
Male	1,175 (56.2)
Female	916 (43.8)
Year specimen submitted	
2011 (August to December)	53 (2.5)
2012	319 (15)
2013	325 (15.5)
2014	348 (16.6)
2015	403 (19)
2016	412 (19.7)
2017 (January to August)	231 (11)
Specimen source	
Respiratory specimens	1,295 (62)
Sputum	631 (30)
Bronchoalveolar lavage fluid	499 (23.8)
Lung tissue	110 (5.2)
Pleural fluid	42 (2)
Tracheal secretions	13 (0.6)
Nonrespiratory specimens	796 (38)
Musculoskeletal	372 (17.8)
Blood	110 (5.2)
Brain biopsy	78 (3.7)
Cerebrospinal fluid	10 (0.4)
Others	226 (10.8)

tion ionization–time of flight mass spectrometry (MALDI-TOF MS) or DNA sequencing are the methods of choice for identification to the species or species complex level (8).

The available data on *Nocardia* species drug susceptibilities are limited, often lack supportive prospective clinical outcomes data, and are usually highly individualized (2). The aim of this work was to perform a retrospective evaluation of *Nocardia* species identified at a tertiary medical center with a reference laboratory over a 6-year period and to provide antimicrobial susceptibility data for the identified *Nocardia* species.

RESULTS

Description of *Nocardia* species isolated. A total of 2,091 cultures were positive for *Nocardia* species from 1 August 2011 through 31 August 2017. Of these, 1,891 (90.4%) were identified to the species level, and 200 (9.5%) were able to be identified only to the genus level as *Nocardia* species. Of the 200 isolates identified only to the genus level, 95 (48%) were identified by partial 16S rRNA gene sequencing, and 105 (52%) were identified by MALDI-TOF MS.

General characteristics of the samples submitted are shown in Table 1. Our sample population included 1,175 (56.2%) men and 916 (43.8%) women. The median age was 66 years (interquartile range, 55 to 76 years). We excluded pediatric samples (any patients 18 years or younger).

Our samples included 22 specimens from international countries. These included 12 samples from Saudi Arabia, 3 from Lebanon, 2 from Qatar, 2 from the United Arab Emirates, 1 from Chile, 1 from Brazil, and 1 from Italy. Among isolates from the United States, 1,056 (50.5%) of the reported specimens were from Florida, Minnesota, Texas, Arizona, Michigan, and Louisiana (300, 256, 143, 135, 114, and 108 specimens, respectively) (Fig. S1 and S2 in the supplemental material).

The number of specimens received per year has steadily increased from 319 in 2012 to 412 in 2016 (Table 1).

The majority of positive cultures were from respiratory specimens (1,295 [62%]), including 631 (30%) from sputum, 499 (23.8%) from bronchoalveolar lavage (BAL) fluid, 110 (5.2%) from lung biopsies, 42 (2%) from pleural fluid, and 13 (0.6%) specimens from

TABLE 2 Results of antibiotic susceptibility testing to *Nocardia* isolates: current study and previous similar studies

	Data for study			
Characteristic	**This study**	**Schlaberg et al. 2014 (9)**	**Valdezate et al. 2017 (10)**	**Lebeaux et al. 2018 (11)**
No. of isolates	2,091	1,299	1,119	736
Patient age (median [IQR]) (yrs)[a]	66 (55–76)	63, DNC	DNC	66 (4–90)
Sex (%)				
Male	56.2	53	DNC	58
Female	43.8	47	DNC	42
Years specimens submitted	2011–2017	2006–2011	2005–2014	2010–2015
Specimen source or reference (no. [%])				
Lung	110 (5.2)	54%	961 (85.9)	427 (53.8)
Sputum	631 (30)	DNC	DNC	156 (19.7)
BAL	499 (23.8)	DNC	DNC	112 (14.1)
Blood	110 (5.2)	6%	13 (1.3)	39 (4.9)
Brain	78 (3.7)	3%	27 (2.8)	37 (4.7)
CSF	10 (0.4)	DNC	DNC	6 (0.8)
Others	653 (31.2)	DNC	DNC	DNC
Antibiotic (% of *N. nova* complex, *N. cyriacigeorgica*, *N. farcinica*, *N. brasiliensis*, N. *abscessus* complex, and *N. transvalensis* complex isolates, respectively, susceptible)				
Amikacin	100, 99, 100, 100, 100, 26	100, 100, 100, 100, 100, 28	100, 99, 98, 100, 100, 52	100, 99, 99, 100, 99, 70
Amoxicillin-clavulanate	4, 8, 96, 99, 61, 89	9, 3, 76, 95, 78, 57	32, 28, 82,92, 96, 100	8, 9, 80, 92, 74, 88
Cefepime	47, 24, 1 ,0, 69, 27	DNC	DNC	77, 65, 9, 44, 92, 83
Ceftriaxone	14, 64, 3, 2, 93, 64	47, 88, 3, 49, 98, 63	DNC	70, 96, 20, 69, 97, 96
Clarithromycin	97, 1, 0, 0, 38, 2	97, 1, 0.5, 3, 29, 4	DNC	DNC
Imipenem	100, 99, 83, 8, 64, 9	99, 43, 33, 1, 31, 6	98, 97, 96, 44, 88, 78	99, 89, 77, 15, 88, 63
Linezolid	100, 100, 100, 100, 100, 100	100, 100, 100, 100, 100, 100	99, 99, 97, 100, 100, 100	100, 100, 100, 100, 100, 100
Minocycline	19, 14, 7, 16, 94, 31	12, 6, 5, 24, 85, 15	11.3, 16,11, 41, 91, 30	93, 81, 87, 87, 98.7, 96
TMP-SMX	100, 100, 99, 100, 100, 88	100, 100, 99.5, 100, 100, 81	80.4, 96, 55, 100, 97, 60	91.7, 97, 96, 96, 98.7, 88
Tobramycin	3, 99, 1, 100, 100, 0	13, 99, 0.5, 100, 100, 4	52, 97, 16, 92, 99, 4	20, 99, 3, 100, 99, 4
Study highlight	Most commonly isolated species (constituting ≈90%) included *N. nova* complex, *N. cyriacigeorgica*, *N. farcinica* complex, *N. brasiliensis*, *N. abscessus* complex, and *N. transvalensis* complex.	More than 90% of isolates belonged to *N. nova* complex, *N. cyriacigeorgica*, *N. farcinica*, *N. brasiliensis*, *N. abscessus* complex, *N. transvalensis* complex, and *Nocardia beijingensis* complex.	Prevalence values for different *Nocardia* species were similar during 2005–2009 and 2010–2014, except for those of *N. abscessus*, *N. farcinica,* and *N. transvalensis*, which fell significantly in the second subperiod ($P < 0.05$).	The most frequent species were *N. farcinica* (20.2%), *N. abscessus* complex (19.9%), and *N. nova* complex (19.5%). The *N. farcinica* proportion increased significantly over time from 13% in 2010 to 27.6% in 2014.

[a]Abbreviations: BAL, bronchoalveolar lavage; CSF, cerebrospinal fluid; CNS, central nervous system; DNC, data not collected; IQR, interquartile range; TMP-SMX, trimethoprim-sulfamethoxazole.

tracheal secretions. Cultures from other sources included musculoskeletal in 372 (17.8%), blood cultures in 110 (5.2%), brain biopsy cultures in 78 specimens (3.7%), and cerebrospinal fluid culture from 10 samples. This is similar to what has been previously described in the literature (Table 2) (9–11).

Table 3 indicates that the most commonly isolated species were *N. nova* complex, 452 (21.6%); *Nocardia cyriacigeorgica*, 352 (16.8%); *N. farcinica* complex, 319 (15.3%); *Nocardia brasiliensis*, 223 (10.7%); *N. abscessus* complex, 205 (9.8%); and *N. transvalensis* complex, 121 (5.8%). These 6 species and species complexes constituted more than 80% of all *Nocardia* species isolated in the study period.

TABLE 3 Identified species for 2,091 *Nocardia* isolates from 2011 to 2017

Species	No. of isolates (%)
Nocardia nova complex[a]	452 (21.6)
Nocardia cyriacigeorgica	352 (16.8)
Nocardia farcinica complex[b]	319 (15.3)
Nocardia brasiliensis	223 (10.7)
Nocardia abscessus complex[c]	205 (9.8)
Nocardia species	200 (9.6)
Nocardia transvalensis complex[d]	121 (5.8)
Nocardia asteroides	76 (3.6)
Nocardia otitidiscaviarum	30 (1.4)
Nocardia pseudobrasiliensis	21 (1)
Nocardia brevicatena/Nocardia paucivorans	19 (0.9)
Nocardia niwae	14 (0.7)
Nocardia puris	9 (0.4)
Nocardia amikacinitolerans	6 (0.3)
Nocardia carnea	5 (0.2)
Nocardia takedensis	5 (0.2)
Nocardia thailandica	5 (0.2)
Nocardia araoensis	4 (0.2)
Nocardia flavorosea	3 (0.1)
Nocardia mexicana	3 (0.1)
Nocardia exalbida	2 (0.1)
Nocardia ignorata	2 (0.1)
Nocardia jiangxiensis	2 (0.1)
Nocardia niigatensis	2 (0.1)
Nocardia testacea	2 (0.1)
Nocardia amamiensis	1 (<0.1)
Nocardia anaemiae	1 (<0.1)
Nocardia blacklockiae	1 (<0.1)
Nocardia brevicatena	1 (<0.1)
Nocardia higoensis	1 (<0.1)
Nocardia higoensis/shimofusensis	1 (<0.1)
Nocardia rhamnosiphila	1 (<0.1)
Nocardia salmonicida	1 (<0.1)
Nocardia shimofusensis	1 (<0.1)
Nocardia sienata	1 (<0.1)
Nocardia vinacea	1 (<0.1)

[a]*N. nova* complex includes *Nocardia africana*, *Nocardia aobensis*, *Nocardia cerradoensis*, *Nocardia elegans*, *Nocardia kruczakiae*, *Nocardia mikamii*, *N. nova*, *Nocardia vermiculata*, and *Nocardia veterana*.
[b]*N. farcinica* complex includes *N. farcinica* and *Nocardia kroppenstedtii*.
[c]*N. abscessus* complex includes *N. abscessus*, *Nocardia arthritidis*, *Nocardia asiatica*, *Nocardia beijingensis*, and *Nocardia pneumoniae*.
[d]*N. transvalensis* complex includes *N. blacklockiae*, *N. transvalensis*, and *Nocardia wallacei*.

Grouping the isolates according to the specimen source submitted, the most common species isolated from respiratory sources (sputum, BAL fluid, lung biopsies, pleural fluid, and tracheal secretions) were *N. nova* complex, 328/1,295 (25.3%); *N. cyriacigeorgica*, 290/1,295 (22.3%); *N. farcinica* complex, 151/1,295 (11.6%); and *N. abscessus* complex, 128/1,295 (9.8%).

The most common *Nocardia* species isolated from brain specimens was *N. farcinica* complex, 33/78 (42.3%), followed by *N. abscessus* complex, 20/78 (25.6%). The most common *Nocardia* species isolated from blood was *N. farcinica* complex, 39/110 (35.4%), followed by *N. nova* complex, 36/110 (32.7%) and *N. cyriacigeorgica*, 16/110 (14.5%).

Table 2 compares our results with other literature reports, and the antimicrobial susceptibility results across the 4 highlighted studies are in good agreement (9–11).

Antimicrobial susceptibility profiles. Antimicrobials *in vitro* susceptibility profiles for some agents were highly variable between different *Nocardia* species (Table 4).

Antimicrobials that generally demonstrated a high level of activity (>90% susceptible [S]) against most *Nocardia* species include amikacin, linezolid, and trimethoprim-sulfamethoxazole (TMP-SMX). All *Nocardia* isolates that were tested against linezolid were susceptible using the current CLSI interpretive criteria.

TABLE 4 Antimicrobial susceptibility profiles by *Nocardia* species

		Susceptibility (%) of indicated species to:												
***Nocardia* species**	***n***	**Amk[a]**	**Amox/clav**	**Cefepime**	**Ceftriaxone**	**Cip**	**Clr**	**Doxycycline**	**Imp**	**Lzd**	**Min**	**Mxf**	**TMP-SMX**	**Tob**
Nocardia nova complex[b]	452	100	4	47	14	1	97	1	100	100	19	3	100	3
Nocardia cyriacigeorgica	352	99	8	24	64	0	1	11	99	100	14	1	100	99
Nocardia farcinica complex[c]	319	100	96	1	3	49	0	2	83	100	7	76	99	1
Nocardia brasiliensis	223	100	99	0	2	0	0	5	8	100	16	40	100	100
Nocardia abscessus complex[d]	205	100	61	69	93	3	38	87	64	100	94	13	100	100
Nocardia species	200	93	37	33	40	14	42	25	76	100	39	39	99	60
Nocardia transvalensis complex[e]	121	26	89	27	64	49	2	10	9	100	31	72	88	0
Nocardia asteroides	76	99	26	51	49	21	51	29	88	100	43	25	100	58
Nocardia otitidiscaviarum	30	100	0	0	0	0	17	43	3	100	60	23	87	53
Nocardia pseudobrasiliensis	21	62	5	0	0	100	95	0	0	100	0	86	33	100
Nocardia brevicatena/Nocardia paucivorans	19	95	47	95	95	100	100	95	100	100	95	84	100	95
Nocardia niwae	14	100	0	7	100	21	100	36	100	100	86	86	100	100
Nocardia puris	9	100	0	0	0	11	0	100	78	100	100	11	100	100
Nocardia amikacinitolerans	6	67	100	17	33	0	0	83	100	100	100	17	100	100
Nocardia carnea	5	100	20	100	100	80	60	20	100	100	40	80	100	100
Nocardia takedensis	5	100	40	100	100	0	100	100	100	100	100	20	100	100
Nocardia thailandica	5	100	0	20	60	0	80	0	100	100	0	20	100	100
Nocardia araoensis	4	100	100	75	100	0	75	25	25	100	25	50	100	100
Nocardia flavorosea	3	100	0	100	100	100	33	67	100	100	67	100	100	100
Nocardia mexicana	3	0	0	0	33	0	0	0	100	100	0	0	0	0
Nocardia exalbida	2	100	0	100	100	0	50	100	100	100	100	0	100	100
Nocardia ignorata	2	100	0	0	0	50	0	100	100	100	100	50	100	100
Nocardia jiangxiensis	2	100	100	0	0	0	100	0	100	100	100	0	100	100
Nocardia niigatensis	2	50	0	0	0	50	50	0	0	100	0	0	50	100
Nocardia testacea	2	100	0	50	100	100	0	0	100	100	0	50	100	100
Nocardia amamiensis	1	100	0	100	100	0	100	100	100	100	100	0	100	100
Nocardia anaemiae	1	100	0	0	100	0	100	0	100	100	100	0	100	100
Nocardia blacklockiae	1	0	100	0	100	0	100	0	100	100	0	100	100	0
Nocardia brevicatena	1	100	0	0	0	0	0	100	100	100	100	0	100	100
Nocardia higoensis	1	100	100	0	0	100	0	100	100	100	100	100	100	100
Nocardia higoensis/shimofusensis	1	100	0	0	0	0	0	0	100	100	0	0	100	100
Nocardia rhamnosiphila	1	100	0	0	0	100	0	0	100	100	0	100	100	100
Nocardia salmonicida	1	100	0	100	100	100	100	100	100	100	100	100	100	100
Nocardia shimofusensis	1	100	0	100	100	100	100	100	100	100	100	100	100	100
Nocardia sienata	1	100	0	0	100	100	0	100	100	100	100	100	100	100
Nocardia vinacea	1	100	0	0	100	0	0	0	100	100	100	0	100	100

[a]AMK, amikacin; Amox/clav, amoxicillin-clavulanic acid; Cip, ciprofloxacin; Clr, clarithromycin; Imp, imipenem; Lzd, linezolid; Min, minocycline; Mxf, moxifloxacin; TMP-SMX, trimethoprim-sulfamethoxazole; Tob, tobramycin.

[b]*N. nova* complex includes *Nocardia africana*, *Nocardia aobensis*, *Nocardia cerradoensis*, *Nocardia elegans*, *Nocardia kruczakiae*, *Nocardia mikamii*, *N. nova*, *Nocardia vermiculata*, and *Nocardia veterana*.

[c]*N. farcinica* complex includes *N. farcinica* and *Nocardia kroppenstedtii*.

[d]*N. abscessus* complex includes *N. abscessus*, *Nocardia arthritidis*, *Nocardia asiatica*, *Nocardia beijingensis*, and *Nocardia pneumoniae*.

[e]*N. transvalensis* complex includes *N. blacklockiae*, *N. transvalensis*, and *Nocardia wallacei*.

In general, susceptibility to amikacin was typical. However, a high rate of resistance (R) to amikacin was noted with *N. transvalensis* complex (74% R) and *Nocardia pseudobrasiliensis* (38% R) and to TMP-SMX with *N. pseudobrasiliensis* (67% R), *Nocardia otitidiscaviarum* (13% R), and *N. transvalensis* complex (12% R).

Imipenem had good *in vitro* activity against *N. cyriacigeorgica* (99% S) and *N. nova* complex (100% S), but high rates of resistance were noted in *N. brasiliensis* (92% R), *N. transvalensis* complex (91% R), and *N. abscessus* complex (36% R).

Ceftriaxone had good *in vitro* activity against *N. abscessus* complex (93% S) and *Nocardia paucivorans* (95% S) but poor activity with *N. farcinica* complex (97% R) and *N. brasiliensis* (98% R).

Amoxicillin-clavulanic acid demonstrated a high level of *in vitro* activity with *N. farcinica* complex (96% S), *N. brasiliensis* (99% S), and *N. transvalensis* complex (~90% S), while this agent performed poorly with *N. nova* complex (96% R) and *N. cyriacigeorgica* (92% R).

Ciprofloxacin had poor *in vitro* activity in general with exception of *N. pseudobrasiliensis* (100% S) and *N. paucivorans* (100% S), while clarithromycin demonstrated good *in vitro* susceptibility against *N. nova* complex (97% S), *N. paucivorans* (100% S), and *N. pseudobrasiliensis* (95% S).

The tetracyclines had good activity only against *N. abscessus* complex (doxycycline, 87% S; minocycline, 94% S) and *N. paucivorans* (doxycycline, 95% S; minocycline, 95% S). Tobramycin demonstrated high *in vitro* activity against *N. cyriacigeorgica* (99% S), *N. brasiliensis* (100% S), *N. abscessus* complex (100% S), *N. pseudobrasiliensis* (100% S), and *N. paucivorans* (95% S). In general, resistance was high for most species against cefepime and moxifloxacin.

Among our 2,091 isolates, we identified 462 isolates (22%) as MDR *Nocardia* species. Of those, >75% belong to *N. brasiliensis* (201[43.5%]), *N. transvalensis* complex (92 [20%]), and *N. farcinica* (56 [12%]).

N. brasiliensis was frequently resistant to imipenem (92% R) and ceftriaxone (98% R) but demonstrated good susceptibility to amikacin, tobramycin, and TMP-SMX.

N. transvalensis complex was frequently resistant to imipenem (91% R) and amikacin (74% R) but retained good susceptibility to amoxicillin-clavulanic acid (89% S) and TMP-SMX (88% S).

In addition, *N. pseudobrasiliensis* was often MDR, with resistance to imipenem (100% R), ceftriaxone (100% R), and TMP-SMX (67% R), but had good susceptibility to ciprofloxacin, clarithromycin, linezolid, and tobramycin.

DISCUSSION

As expected, the most common source for positive *Nocardia* cultures was respiratory sources. *Nocardia* species were recovered from blood cultures in about 5% and from brain biopsies in 3.7% of patients with suspected nocardiosis.

Most of our patient population were of older age with a median age of 60 years, and the highest number of specimens were sent from southern states, including Florida, Texas, Louisiana, and Arizona (with the exception of high numbers from Minnesota and Michigan). This may be a reflection of geographic differences in *Nocardia* distribution, or it could be due to the location of laboratories using the Mayo Clinic as a reference laboratory.

We also noted a steady increase in the number of specimens over the study time frame, which might indicate an increasing incidence or, alternatively, more awareness of the need for, and easier access to, *Nocardia* culture and antimicrobial susceptibility testing.

The susceptibility profiles of *Nocardia* species against the antimicrobials recommended by the CLSI for *in vitro* susceptibility testing were highly variable by agent and by species, demonstrating the need to routinely identify *Nocardia* isolates to the species level and to perform *in vitro* susceptibility testing for all isolates thought to be clinically significant. In general, amikacin, linezolid, and TMP-SMX demonstrated good *in vitro* activity against most *Nocardia* species, and these agents are often used in combination empirically while awaiting laboratory susceptibility testing results. Possible exceptions to this rule are *N. pseudobrasiliensis* and *N. transvalensis* complex, which can show variable susceptibility to amikacin and sometimes TMP-SMX *in vitro*.

To our knowledge, this report provides the largest data set to date on the epidemiology and antimicrobial susceptibility profiles of *Nocardia* isolates from across the United States and worldwide and is consistent in many aspects with previously published reports (Table 2) (9, 10, 12).

The time between the isolation of *Nocardia* species and the availability of susceptibility results can be several weeks, so the choice of empirical antibiotic regimen can be aided by the *in vitro* data provided in this report and in previously published reports while awaiting completion of laboratory testing.

MATERIALS AND METHODS

The study was approved by the Mayo Clinic Institutional Review Board. A retrospective review of laboratory data was conducted to identify microbiologic cultures from adult patients who were positive for *Nocardia* species in the period between 1 August 2011 and 31 August 2017 and for which antimicrobial susceptibility testing was performed.

The clinical microbiology laboratory at Mayo Clinic in Rochester, Minnesota, receives specimens for microbiologic culture, identification, and susceptibility testing from Mayo Clinic hospitals and from Mayo Clinic Laboratory client hospitals throughout the United States and from many countries throughout the world.

Specimens received were cultured in BD Bactec mycobacteria growth indicator tube (MGIT) 960 broth in mycobacterial growth indicator tubes (Becton, Dickinson and Company, Franklin Lakes, NJ) and on Middlebrook 7H11/7H11S agar biplates incubated at 35 to 37°C for up to 6 weeks. Positive MGIT broth was subcultured to a Middlebrook 7H11 agar plate, and isolated colony growth was identified using Sanger sequencing of a 500-bp region of the 16S rRNA gene as previously described (13). Databases used included the MicroSeq ID 16S rDNA 500 library with the current version for the year the isolate was identified from 2011 to 2017 and a Mayo Clinic custom database containing well-characterized clinical isolates and type strains with multiple strains per species in order to augment strain diversity found in the MicroSeq database, and, if neither the MicroSeq nor the Mayo database provided a match, NCBI GenBank BLAST analysis was used with the sequence required to be published in peer-reviewed literature in order to accept the result. A 100% match to the database entry was required for identification. Sequence length was required to be at least 420 bp, and the Phred quality score was required to be >30. In 2015, the use of MALDI-TOF MS was added to supplement species identification using Sanger sequencing (14).

Antimicrobial susceptibility testing was performed using CLSI guidelines current during the study period (15), and the Trek Sensititre Rapmyco plate was used for rapidly growing mycobacteria and *Nocardia* species. Interpretation of the minimal inhibitory concentration (MIC) as susceptible or resistant for each isolate was done using current CLSI interpretive criteria (16). MICs reported as intermediate (I) were combined with resistant (R) for this study.

Taxonomy. A recent review by Conville et al. (7) was used to determine the most current taxonomy for *Nocardia* species. Thus, the *Nocardia abscessus* complex includes *N. abscessus*, *Nocardia arthritidis*, *Nocardia asiatica*, *Nocardia beijingensis*, and *Nocardia pneumoniae*. The *Nocardia nova* complex includes *Nocardia africana*, *Nocardia aobensis*, *Nocardia cerradoensis*, *Nocardia elegans*, *Nocardia kruczakiae*, *Nocardia mikamii*, *N. nova*, *Nocardia vermiculata*, and *Nocardia veterana*. The *Nocardia farcinica* complex includes *N. farcinica* and *Nocardia kroppenstedtii*. The *Nocardia transvalensis* complex includes *Nocardia blacklockiae*, *N. transvalensis*, and *Nocardia wallacei*.

Multidrug-resistant *Nocardia*. To our knowledge, there is no current consensus for defining multidrug-resistant (MDR) *Nocardia*, but in this work, the definition by Schlaberg et al. (9) was followed, with MDR *Nocardia* species defined as an isolate that is nonsusceptible (resistant or intermediate) to 2 or more of the most commonly used empirical agents, which would currently be amikacin, ceftriaxone, imipenem, and TMP-SMX.

SUPPLEMENTAL MATERIAL

Supplemental material is available online only.

SUPPLEMENTAL FILE 1, PDF file, 0.4 MB.

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