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A multicentre analysis of *Nocardia* pneumonia in Spain: 2010–2016

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ABSTRACT

Objective: To analyse all cases of *Nocardia* pneumonia occurring between 2010 and 2016 in five Spanish hospitals.
Methods: This was a retrospective observational analysis of clinical and microbiological data collected from 55 cases of *Nocardia* pneumonia.
Results: There were one to 20 cases per hospital and six to nine cases per year. Chronic obstructive pulmonary disease, bronchiectasis, and asthma were the main predisposing underlying respiratory conditions. Thirty-four patients were receiving systemic and/or inhaled corticosteroids prior to infection, eight had neoplasia, and six had haematological malignancies. Clinical and radiological findings were common to pneumonia of other infectious aetiologies, except for the frequent presence of nodules and cavitation. Overall, the 1-year mortality was high (38.2%), and mortality was directly related to the pulmonary disease in 15 patients (27.3%). The most frequently identified species were *N. cyriacigeorgica* ($n = 21$), *N. abscessus* ($n = 8$), and *N. farcinica* ($n = 5$). All *Nocardia* isolates were susceptible to linezolid and all but two were susceptible to amikacin and trimethoprim–sulfamethoxazole.
Conclusions: Nocardia pneumonia-associated mortality remains high, probably because of the debilitated status of patients in whom this pathogen is able to cause pulmonary infection.

Introduction

Nocardia species are gram-positive aerobic actinomycetes commonly found in soil. To date, 119 *Nocardia* species have been described (Parte, 2018), and although all are potentially pathogenic (Ercibengoa et al., 2016), only a small proportion have been described as responsible for human infections. According to the

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anatomical localization, nocardiosis can be divided into pulmonary, disseminated (including central nervous system (CNS) involvement), and cutaneous (Minero et al., 2009). Human pulmonary infections are acquired mainly through the respiratory route by inhalation of the bacteria; however, most infections are limited to transient colonization, and *Nocardia* acts as a pathogen only on some occasions (Brown-Elliott et al., 2006). Pulmonary nocardiosis at presentation is subacute (Singh et al., 2016) and usually occurs in immunocompromised patients or in patients with chronic underlying pulmonary diseases (Kurahara et al., 2014; Minero et al., 2009; Muñoz et al., 2007; Steinbrink et al., 2018). Clinically, *Nocardia* pneumonia is indistinguishable from pneumonia caused by other infectious agents, making it very difficult to suspect nocardiosis in the immunocompetent population (Fujita et al., 2016; Kim et al., 2016; Steinbrink et al., 2018). Cell-mediated immunity seems to be crucial for preventing the dissemination of *Nocardia* from the portal of entry into the rest of the body. Consequently, patients on corticosteroid therapy and those on other therapies or with diseases causing cellular immunosuppression are at a higher risk of suffering from an invasive or disseminated *Nocardia* infection (Kontoyiannis et al., 1998).

In their report published in 1997, Menendez et al. established that the diagnosis of pulmonary nocardiosis was difficult and usually delayed. Moreover, it was frequently disseminated to other body parts, and a combined, synergistic antimicrobial treatment as initial therapy was proposed (Menéndez et al., 1997). Since then, new *Nocardia* diagnostic and molecular identification methods, as well as new antibiotics for the treatment of nocardiosis have been introduced in clinical practice (McTaggart et al., 2010; Moylett et al., 2003). In this study, all *Nocardia* pneumonia cases diagnosed in Spain over a 7-year period were reviewed, thus providing a large, recent, real-life multicentre series of this infrequent infection.

Methods

Patients

The study included all cases of *Nocardia* pneumonia occurring between 2010 and 2016 in five tertiary Spanish hospitals in three different cities (Madrid, Barcelona, and San Sebastian). The inclusion criteria for a case of *Nocardia* pneumonia were the presence of a radiological image compatible with pneumonia and a *Nocardia* spp cultured from a respiratory secretion and identified as the pathogen responsible for the infection.

Clinical and microbiological data were reviewed retrospectively and recorded according to a previously designed questionnaire; these included the patients' conditions and risk factors, as described in Table 1.

Ethics

The work was done according to the regulatory requirements of the Spanish legislation in force (Ley Organica 3/2018) and data were processed and analysed anonymously. Publication of the results of this study was approved by the Clinical Research Ethics Committee of the Basque Country (reference 2017161).

Microbiological studies

All isolates were presumptively identified as *Nocardia* according to their phenotypic growth characteristics. Definitive species identification was performed by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS; Bruker Daltonics, Germany) after direct transfer–formic acid preparation and a species cut-off score value of >1.7, or by sequencing a fragment of the 16S rRNA (Steingrube et al., 1997), *hsp65* (Telenti et al., 1993), and *secA1* (Conville et al., 2006) genes. A ≥ 99% similarity with the corresponding sequences of the reference species available in GenBank (http://www.ncbi.nlm.nih.gov) was required for species identification (CLSI (Clinical and Laboratory Standards Institute), 2018).

Susceptibility testing was performed at each of the participating hospitals by broth microdilution method using Sensititre microtitre trays (Thermo Fisher, Inc., West Sussex, UK) or by Etest (AB Biodisk, Solna, Sweden). *Staphylococcus aureus* ATCC 29213 was used as control. Antibiotics tested in each hospital varied, but trimethoprim–sulfamethoxazole (TMP–SMZ), imipenem, amikacin, linezolid, and ciprofloxacin were tested in all participating hospitals. Minimum inhibitory concentrations (MICs) were recorded and interpreted according to the Clinical and Laboratory Standards Institute (CLSI) interpretative criteria for *Nocardia* (CLSI (Clinical and Laboratory Standards Institute), 2011).

Table 1
Main predisposing conditions studied in 55 patients with *Nocardia* pneumonia.

	Number	%
Respiratory conditions		
COPD	20	36.4
Bronchiectasis	16	29.1
Asthma	7	12.7
Lung carcinoma	2	3.6
Previous pneumonia	2	3.6
Other conditions		
Cardiovascular disease	18	32.7
Diabetes	10	18.2
Chronic renal failure	9	16.4
Neoplasia[a]	7	12.7
Haematological malignancies	6	10.9
Liver disease	5	9.1
HCV infection	2	3.6
Chronic gastritis	1	1.8
Immunosuppression		
Systemic corticosteroids	29	52.7
Inhaled corticosteroids	22	40.0
HIV infection	5	9.1
Haematopoietic stem cell therapy	4	7.3
Risk habits		
Alcoholic or ex	6	10.9
Smoker or ex	21	38.2
IVDU or ex	3	5.5
Delay to treatment initiation		
Symptoms to treatment (days) mean ± SD[b]	11.45 ± 14.01	
RX diagnosis to treatment (days) mean ± SD[c]	6.29 ± 11.97	

COPD, chronic obstructive pulmonary disease; HCV, hepatitis C virus; IVDU, intravenous drug user; SD, standard deviation; RX, radiological; CNS, central nervous system.
[a] CNS (n = 2), kidney, prostate, rectal, anal, colon.
[b] Data corresponding to 44 patients.
[c] Data corresponding to 48 patients.

Statistical analysis

Frequencies of categorical variables were compared using the Chi-square test or Fisher's exact test, as appropriate. A univariate logistic regression analysis was performed to calculate the relationship between each of the conditions included in Table 1 and pneumonia mortality. In this analysis, patients who died because of other causes were excluded. The variables that resulted in a p-value of <0.20 level of significance were analysed using a multivariate logistic regression model. The final selection of variables associated with mortality was made with the backward stepwise selection method. The statistical analyses were performed using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA).

Table 2
Annual distribution of the cases of *Nocardia* pneumonia recorded in five Spanish hospitals, 2010–2016.

Total	2010	2011	2012	2013	2014	2015	2016	Total
N. abscessus	1	1	2	2	0	0	2	8
N. arthritidis	0	0	0	0	0	1	0	1
N. beijingensis	0	0	0	0	0	0	1	1
N. cyriacigeorgica	3	2	2	4	4	3	3	21
N. farcinica	0	0	1	1	1	1	1	5
N. otitidiscaviarum	2	0	1	0	1	0	0	4
N. pseudobrasiliensis	0	0	1	0	0	0	0	1
N. wallacei	0	1	0	0	0	0	0	1
Nocardia spp	1	3	1	1	0	2	0	8
N. transvalensis	0	2	1	0	0	0	1	4
N. veterana	1	0	0	0	0	0	0	1
Total	8	9	9	8	6	7	8	55

Results

Overall, 55 patients fulfilled the criteria for *Nocardia* pneumonia. The average age at the time of infection was 67.5 years (range 23–90 years) and 35 (63.6%) were male.

The number of patients varied greatly among hospitals, from one to 20. However, the overall number of cases per year was very homogeneous, ranging from six cases in 2014 to nine cases in 2011 and 2012 (Table 2). Most patients (52/55, 94.5%) had predisposing respiratory factors for developing pneumonia and many were immunocompromised as a result of disease or pharmacological treatment (Table 1).

Clinical manifestations

The average duration of infection from the onset of symptoms to diagnosis, registered in 24 patients, was 12.9 days (range 2–34 days). Cough and purulent expectoration were the most frequent clinical manifestations (Table 3).

The infection was disseminated to the CNS in two patients. The time-to-diagnosis in these two patients was slightly longer than the average of the rest of the patients (28 and 34 days). The first case of CNS involvement was a *N. cyriacigeorgica* infection in a 23-year-old woman who eventually died because of acute megaloblastic leukaemia. The second case was caused by a *Nocardia* spp (not identified to the species level) in a 25-year-old man, ex-intravenous drug user (IVDU), who was infected with hepatitis C virus (HCV) and HIV and was not on antiretroviral therapy (1×10^9 leukocytes/l, 1% CD4 count, 91 710 HIV copies/ml). His initial TMP–SMZ treatment was changed to oral linezolid 600 mg/12 h and meropenem 2 g/8 h intravenously (IV) due to a cutaneous rash. Meropenem was replaced after 30 days with ceftriaxone IV 1 g/24 h and the patient recovered.

Table 3
Clinical manifestations in 55 patients with *Nocardia* pneumonia.

Clinical manifestations	Number	%
Cough	39	71
Purulent expectoration	39	71
Fever	25	45.5
Dyspnoea	19	34.5
Fatigue	14	25.5
Pleuritic pain	11	20
Confusion	5	9.1
Sweating	3	5.5
Weight loss	1	1.8

Pulmonary radiological findings

The most common radiological finding was consolidation ($n = 33$), followed by nodules ($n = 27$), cavitation ($n = 14$), bronchiectasis ($n = 6$), and infiltrates ($n = 4$). Fibrotic tracts were observed in two patients, an interstitial lung pattern in one patient, and ground glass opacities in one patient.

Consolidation was the only radiological finding in 10 patients; consolidation was observed together with nodules in eight patients, with nodules plus cavitation in five patients, with pleural effusion in three patients, and with cavitation and pleural effusion in two patients. In total, four patients presented pleural effusion, three of whom were infected with *N. abscessus*.

The presence of consolidation with nodules and/or cavitation was not associated with any specific *Nocardia* species. Still, seven out of nine (77.8%) patients with *N. farcinica* or *N. otitidiscaviarum* pneumonia had consolidation with nodules (three and one of them with cavitation, respectively). However the high presence of nodules in pneumonia caused by *N. farcinica* and *N. otitidiscaviarum* compared to the rest of the species (18/46, 39.1%) did not reach statistical significance ($p = 0.063$). Cavitation was found in 13 of 41 immunocompromised patients and in one of 13 immunocompetent patients ($p = 0.146$). The two patients with lung carcinoma showed cavitation; it was not possible to determine whether the cavitation was due to the carcinoma or to the *Nocardia* infection.

Treatments and outcomes

The 1-year mortality associated with *Nocardia* pneumonia was high: 38.2% (21/55). The 30-day all-cause mortality after a *Nocardia* pulmonary diagnosis was 18.2% (10/55). Overall, six deaths were not directly related to the *Nocardia* pneumonia but to the underlying disease: HIV, massive bleeding in a cirrhotic patient, cardiac insufficiency, leukaemia, anal neoplasia, and astrocytoma. In the other 15 cases, mortality was related to the lung disease that occurred in the patients, all of whom were receiving corticosteroids at the time of infection (one inhaled, five systemic, and nine both). Furthermore, seven had chronic obstructive pulmonary disease (COPD) (one with bronchiectasis and asthma), two only bronchiectasis, three were on haematopoietic stem cell therapy (one of whom also had COPD), two had neoplasia (glioblastoma and pulmonary adenocarcinoma), one had cryptogenic organized pneumonia, and the last one was an 85-year-old man with no pulmonary underlying disease but with cardiovascular disease and hepatomegaly.

To investigate the influence of the different risk factors on mortality, the six patients who died of causes not directly related to the pneumonia and one survivor for whom most clinical data were not available were excluded from the analysis. Of all risk factors described in Table 1, only four showed a p-value of <0.2 in the univariate analysis (Table 4). The multivariate analysis demonstrated that having systemic corticosteroids ($p = 0.002$) was the only individual risk factor associated with mortality. The systemic corticosteroids administered varied greatly between patients in terms of the type, dosage, and combinations. Twelve patients were receiving methylprednisolone, 11 prednisone, five dexamethasone, and one deflazacort at the time of infection. Being a smoker or former smoker, having inhaled corticosteroids, and being on haematopoietic stem cell therapy, although having a p-value of <0.2 in the univariate analysis, did not show an association with mortality in the multivariate analysis ($p = 0.376$, $p = 0.383$, $p = 0.106$, respectively). A delay in initiating the antibiotic treatment, from symptom onset or from radiological diagnosis, was not associated with mortality in the univariate analysis ($p = 0.459$ and $p = 0.535$, respectively).

Table 4
Significant risk factors for mortality in the logistic regression analyses ($n = 48$).

	Univariate[a]			Multivariable		
Variable	OR	95% CI	*p*-Value	OR	95% CI	*p*-Value
Inhaled corticosteroids	4.00	1.10 to 14.60	0.036	-	-	-
Systemic corticosteroids	28.00	3.25 to 241.34	0.002	28.00	3.25 to 241.34	0.002
Haematopoietic stem cell therapy	8.00	0.76 to 84.59	0.084	-	-	-
Current smoker or ex-smoker	2.63	0.75 to 9.24	0.132	-	-	-

OR, odds ratio; CI, confidence interval. Data are shown as the estimated OR (95% CI) of the explanatory variables in the mortality group. OR is defined as the probability of being in the mortality group divided by the probability of being in the non-mortality group. The *p*-values are based on the null hypothesis that all ORs relating to an explanatory variable equal unity (no effect).
[a] The variables analysed in the univariate analysis were those described in Table 1.

Excluding the patients who died, the average length of treatment was 6.3 months (range 3–13 months, median 6 months). Forty-three patients were treated with TMP–SMZ, either alone (23 patients) or in combination (20 patients) with other antibiotics. The most frequent combination was TMP–SMZ with imipenem/meropenem (11 patients), in five of them also with amikacin. Linezolid was used in three patients (alone in two patients and in combination with meropenem in one patient) due to secondary effects to TMP–SMZ (rash and renal tubular acidosis) or in vitro suspected *Nocardia* TMP–SMZ resistance. In the two patients treated with linezolid alone, the duration of treatment was 5 months and 7 months, respectively. The first patient had to stop his treatment because of polyneuropathy, but was considered cured.

Excluding the six deaths not directly related to the *Nocardia* pneumonia, there was no difference in the survival of patients with pulmonary nocardiosis treated with only TMP–SMZ compared to other antibiotic treatments: 5/15 (33.3%) patients died and 15/34 (44.1%) survived ($p = 0.54$).

Antimicrobial susceptibility

The *Nocardia* was isolated from the sputum of 42 patients, from the bronchoalveolar lavage or aspirate (BAL/BAS) of 10 patients, and from the tracheal aspirate, transthoracic biopsy, and pleural fluid of one patient each.

Antimicrobial susceptibility results were available for 49 isolates, with all being susceptible to linezolid and all but two, one *N. farcinica* and one *N. otitidiscaviarum*, being susceptible to amikacin (Table 5). There were two TMP–SMZ-resistant isolates: one *N. otitidiscaviarum* and one *Nocardia* spp (not identified to the species level). Half of the *N. abscessus* and *N. otitidiscaviarum* were imipenem-resistant, while nearly all isolates of other species were susceptible to carbapenems. Fluoroquinolones were the antibiotics

Table 5
Susceptibility criteria and range, MIC_{50} and MIC_{90}, and number of susceptible isolates of the *Nocardia* species most frequently found in cases of pneumonia in Spain, 2010–2016.

Species	Number		Amikacin	Ciprofloxacin	Imipenem	Linezolid	TMP–SMZ
Susceptible criteria			≤8	≤1	≤4	≤8	≤2/38
N. cyriacigeorgica	21	Range	≤1–1.5	1–>4	≤2–64	≤1–2	≤0.25–1
		MIC_{50}	≤1	>4	≤2	≤1	≤0.25
		MIC_{90}	≤1	>4	4	≤1	≤1
		S[a]	21/21	2/20	19/21	21/21	21/21
N. abscessus	8	Range	≤1	0.12–>4	≤2–>64	≤1	≤0.25–0.5
		MIC_{50}	≤1	4	4	≤1	≤0.25
		MIC_{90}	≤1	>4	>64	≤1	0.5
		S[a]	8/8	1/7	4/8	7/7	8/8
N. farcinica	5	Range	≤1–16	1–4	≤2–>64	≤1–4	0.5–2
		MIC_{50}	≤1	4	≤2	≤1	0.5
		MIC_{90}	16	>4	12	4	2
		S[a]	4/5	1/4	2/4	5/5	5/5
N. otitidiscaviarum	4	Range	≤1–16	1–>4	≤2–32	≤0.5–2	≤0.25–4
		MIC_{50}	≤1	1	≤2	0.5	0.5
		MIC_{90}	16	>4	32	2	4
		S[a]	3/4	2/4	2/4	4/4	3/4
N. transvalensis	4	Range	≤1–4	0.25–>4	≤2	≤1	≤0.25–0.5
		MIC_{50}	≤1	0.25	≤2	≤1	≤0.25
		MIC_{90}	4	>4	≤2	≤1	0.5
		S[a]	4/4	3/4	4/4	4/4	4/4
Nocardia (all)[b]	49	Range	0.06–16	≤2–64	≤2–>64	≤1–4	≤0.25–32
		MIC_{50}	≤1	>4	≤2	≤1	0.25
		MIC_{90}	2	>4	64	≤1	2
		S[a]	47/49	11/45	31/41	47/47	47/49

MIC, minimum inhibitory concentration; TMP–SMZ, trimethoprim–sulfamethoxazole.
[a] Number of susceptible isolates of all tested.
[b] Including 21 *N. cyriacigeorgica*, 8 *N. abscessus*, 5 *N. farcinica*, 4 *N. otitidiscaviarum*, 4 *N. transvalensis*, 4 *Nocardia* spp, and one each *N. arthritidis*,*N. beijingensis*, and *N. veterana*.

with the highest rates of resistance (75% resistant isolates), mainly due to the predominance of *N. cyriacigeorgica* infections in the population of this study.

Discussion

The respiratory tract is the main portal of entry for *Nocardia*, and as a consequence, around 50% to 70% of nocardiosis patients have pulmonary involvement (Ambrosioni et al., 2010; Hashemi-Shahraki et al., 2015; Minero et al., 2009; Uhde et al., 2010). Pulmonary nocardiosis has a low incidence, and the incidence in Spain has been maintained at a regular level over the past decade (Minero et al., 2009). In this study, performed between 2010 and 2016, the incidence of pulmonary nocardiosis varied greatly among hospitals, from one to 20 cases. However, the total number of annual cases was quite uniform, without the presence of any outbreak. *N. cyriacigeorgica* was the most prevalent species causing pneumonia, followed by *N. abscessus* and *N. farcinica*, a species distribution similar to other Spanish studies (Minero et al., 2009; Portolá et al., 2009; Valdezate et al., 2017). The absence of any pulmonary infection caused by *N. nova* was surprising, as this species is common in Spain and other countries (Lebeaux et al., 2019; Uhde et al., 2010; Valdezate et al., 2017).

Pulmonary nocardiosis commonly affects debilitated patients with predisposing conditions, especially those who are immunocompromised due to organ transplantation and/or corticosteroid treatment and COPD patients (Ambrosioni et al. 2010; Singh et al., 2016; Steinbrink et al., 2018; Takiguchi et al., 2017; Ott et al., 2019). In the present study, all 55 patients with *Nocardia* pneumonia had an immunological or respiratory predisposing factor. Overall mortality (38.2%) and mortality directly related to *Nocardia* pneumonia (27.3%) was between the 18.9% and 56.7% mortality described in similar series (Muñoz et al., 2007; Singh et al., 2016; Steinbrink et al., 2018; Takiguchi et al., 2017; Ott et al., 2019). Systemic corticosteroid therapy was the only individual risk factor associated with mortality in the univariate and multivariate analysis. Some authors have not found any differences in the treatment outcome between immunocompetent and immunocompromised patients (Kim et al., 2016), although in other works an increase in the rate of disseminated infections and higher mortality have been observed in immunocompromised patients (Steinbrink et al., 2018).

Radiological findings in patients with pulmonary nocardiosis did not differ from those of patients with pneumonia caused by other respiratory pathogens, except for the presence of nodules in 26 of the 55 patients, a common radiological picture described previously (Singh et al., 2016; Steinbrink et al., 2018; Yang et al., 2014). Nodules were not significantly more frequent in pneumonia caused by any particular *Nocardia* species, although *N. farcinica* and *N. otitidiscaviarum* showed a tendency towards causing nodules more commonly. Other studies have found an increased proportion of cavitation in immunocompromised hosts (Kim et al., 2016; Steinbrink et al., 2018). In the present study, although all but one of the 14 patients with cavitation were immunocompromised, this difference was not significant compared to immunocompetent patients.

Clinical manifestations were very similar to those observed in pneumonia of other aetiologies, except for the lack of fever in more than half of the patients, which could be suggestive of pulmonary nocardiosis (Steinbrink et al., 2018). Despite the high rate of immunocompromised patients, disseminated infections were identified in only two patients, both in the CNS, a rate similar to that described by Kurahara et al. (2014), but much lower than is commonly observed (Ott et al., 2019; Singh et al., 2016; Steinbrink et al., 2018). In these two severely immunocompromised patients, the time-to-diagnosis was around 1 month, a delay that could have favoured dissemination of the infection to the brain.

No association between mortality and a delay in initiating the antibiotic treatment was observed, which has been suggested in other works as a risk factor for developing *Nocardia* pneumonia (Singh et al., 2016; Yang et al., 2014). TMP–SMZ resistance has also been identified as an independent and significant risk factor for overall mortality in pulmonary nocardiosis (Kurahara et al., 2014). In our study, TMP–SMZ was the treatment used for most patients, either alone or in combination with carbapenems or amikacin, despite which the mortality rate was high. As in other studies (Muñoz et al., 2007), patient outcomes were not related to the antibiotic prescribed, which suggests that in the prognosis of *Nocardia* pneumonia, other factors such as underlying diseases or clinical and immunological status at the time of infection have more influence than the antibiotics used in the treatment.

Most *Nocardia* isolates causing pneumonia showed in vitro susceptibility to the majority of antimicrobials used for treatment, such as linezolid or TMP–SMZ. Imipenem resistance was strongly related to *N. abscessus* and *N. otitidiscaviarum*, while nearly all isolates of other species were susceptible, as has been described previously (Larruskain et al., 2011; Muñoz et al., 2007; Uhde et al., 2010). Most *Nocardia* isolates – 75.6% – were ciprofloxacin-resistant, a percentage of resistance higher than reported in the United States (Uhde et al., 2010), but similar to reports from Spain (Larruskain et al., 2011). In contrast, the prevalence of TMP–SMZ resistance, at 4.1%, was lower than the 10.8–42% described in some studies (Minero et al., 2009; Uhde et al., 2010; Valdezate et al., 2017). Although *N. farcinica* is among the species more frequently resistant to TMP–SMZ (Minero et al., 2009; Kurahara et al., 2014; Valdezate et al., 2017), in the present study all five *N. farcinica* isolates were susceptible.

The main limitation of this study is its retrospective design, which meant that some cases could have been lost, and some data, like the species identification or the antimicrobial susceptibility of some of the isolates, could not be determined. Also, the retrospective design made it impossible to evaluate the severity of COPD in patients with this disease and consequently the influence of *Nocardia* pulmonary infections in their outcomes. The stringent conditions used for patient recruitment (presence of radiologically confirmed pneumonia and the isolation of a *Nocardia* in good quality respiratory samples) could have biased the study towards more ill patients, excluding milder cases of *Nocardia* pneumonia in the population with fewer underlying conditions. Finally, the low number of cases for the statistical analyses, the wide range of the confidence intervals, and the low numbers of variables included in the multivariate analysis imply that the results should be interpreted with caution.

In conclusion, this study gathered one of the largest series of *Nocardia* pneumonia, which usually occurs in patients with underlying pulmonary conditions or immunosuppression. The progression of disease was not associated with the antibiotic therapy used. In Spain, *N. cyriacigeorgica* was the most prevalent species causing pneumonia and was susceptible to most antibiotics used in *Nocardia* treatment.

Conflict of interest

None.

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