

Letter to the Editor

Isolation frequency and susceptibility patterns of *Nocardia* species at a tertiary hospital laboratory in Karachi, Pakistan

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Key words: *Nocardia*; sensitivity pattern; Co-trimoxazole; Pakistan

J Infect Dev Ctries 2011; 5(6):499-501.

(Received 9 June 2010 - Accepted 24 January 2011)

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Nocardia species are ubiquitous, fine, soil-borne aerobic filamentous actinomycetes that are Gram positive and weakly acid fast [1]. Nocardiosis is an important opportunistic infection caused by *Nocardia* species. The infection most often occurs in immunocompromised individuals, especially those deficient in cell-mediated immunity but cases of nocardiosis have also been reported in some immunocompetent individuals [1,2]. Person-to-person transmission of *Nocardia* has not been reported in the literature and the organism is usually considered to be acquired from the environment [1,3]. Pulmonary nocardiosis and traumatically induced local abscesses are the common clinical manifestations of infection although rare cases of bacteremia, peritonitis, and corneal ulcers due to *Nocardia* species have also been reported [4-7]. Clinical diagnosis of nocardiosis is often difficult and misleading because of its relative low incidence and lack of pathognomonic symptoms [1,8]; hence the diagnosis is usually based on the isolation of the organism in pure culture from the affected area [9].

While many studies have been conducted worldwide to investigate the prevalence of nocardiosis in different regions [4,5,10], none have been performed in Pakistan; only limited individual case reports have been described from our country [11,12,13]. Our study was conducted to assess the frequency of infection by and sensitivity patterns of different *Nocardia* species isolated over a 15-year period at the Microbiology Laboratory of Aga Khan University Hospital, which is one of the leading tertiary care hospitals in Karachi. The Microbiology Laboratory services comprise a main clinical

laboratory and a network of collection points all over Pakistan; hence the data represent patients throughout the country.

Cases of nocardiosis were identified using the hospital's computerized database for positive specimens submitted during the period 1990-2005, and reviewing the laboratory records of all these patients. Standard isolation and identification techniques as described by the American Society of Microbiology (ASM) were used for the diagnosis of nocardial infections [14]. Blood agar and chocolate agar were used for isolation, and identification was performed on the basis of colonial morphology, microscopic morphology (Gram stain and partial acid-fast stain) and biochemical tests (casein, tyrosine, xanthine and urea hydrolysis). Antimicrobial sensitivity was performed using the Kirby-Bauer disk diffusion method [15].

A total of 922,950 specimens were submitted to the laboratory, comprised of 497,533 (53.9%) samples from males and 425,417 (46.1%) samples from females. *Nocardia* species were isolated from 120 (0.013%) clinical specimens.

A total of 120 cases of nocardiosis were observed during the 15-year period studied, showing an isolation frequency of eight cases per year. This isolation frequency is comparable to that of European countries [10,16,17], but it is quite low when compared to countries sharing similar climatic conditions as ours, such as Japan and parts of the United States [1,18]. One of the reasons for lower isolation rates in our study might be that clinical diagnosis of nocardiosis is often difficult and a strong degree of suspicion is required for proper diagnosis

Table 1. Distribution of *Nocardia* spp. with respect to patient age.

Age	n (%)
< 5 years	6 (5.0%)
5-20 years	9 (7.5%)
20-40 years	31(25.8%)
40-60 years	41(34.2%)
> 60 years	33 (27.5%)

[8]. Similarly, isolation of *Nocardia* species from clinical specimens requires a long incubation period so many cases may go unidentified when there is no early suspicion of nocardiosis by the clinician [8]. Recent reports also suggest an increasing incidence of nocardiosis [7], but in our study we observed 6-10 cases each year and the incidence remained almost constant throughout the 15-year study.

Eighty-three (69%) samples that yielded the growth of *Nocardia* species were from hospitalized patients while the remaining 37 (31%) samples were submitted to the laboratory through an outside referral. This higher isolation in hospitalized patients may reflect the severity of disease or the presence of some underlying conditions in patients which may be associated with the development of nocardiosis; however, as the clinical data of these patients could not be reviewed, this hypothesis could not be investigated.

Isolation of *Nocardia* was significantly higher (p-value < 0.05 using chi-square test for comparison according to gender) in males (68%) as compared to females (32%). These findings are similar to most of the published literature [6,10,16,17]. No definitive explanation for this predominance in the male sex has yet been described but researchers believe that this could be due to hormonal effects on the virulence of organisms [1].

Patients ranged in age from less than one year to 95 years. The number of identified cases increased gradually with increasing age, with the maximum number of cases observed between the ages of 40-60 years. The number of cases declined in individuals older than 60 years of age (Table 1).

The clinical spectrum of nocardiosis was similar to that reported in the literature, with the respiratory tract cited as the most common site of isolation (58.3%) followed by wound infections (35%). Blood culture was positive in 3.3% cases while ocular nocardiosis was observed in 2.5%. Cerebrospinal

fluid (CSF) involvement was uncommon in our study and was seen only in one case (0.8%). These findings are similar to the results of other studies except for the involvement of CSF which was lower in our study as compared to other studies [16-18].

Among 120 isolated strains of *Nocardia*, 87 (72.5%) were identified as *Nocardia asteroides*, 13 (10.8%) as *Nocardia otitidiscaviarum* and 11 (9.2%) as *Nocardia caviae*. Nine (7.5%) strains could not be identified to the species level using conventional methods. Similar distributions of *Nocardia asteroides* and *Nocardia otitidiscaviarum* are described elsewhere in the literature [1,16-18]. *Nocardia caviae* is not a common pathogen but in our study it was isolated in 9.2% of cases; this could be due to geographical variation in the distribution of the organism.

In vitro susceptibility testing of *Nocardia* species isolates from patients showed imipenem (100%) and amikacin (99%) to be the most effective treatment choice for nocardial infections. Sensitivity to cotrimaxazole, ofloxacin, amoxicillin-clavulanic acid and erythromycin was 76.5%, 60%, 45.3% and 24% respectively. Although cotrimaxazole is considered the drug of choice for the treatment of nocardial infections, a moderate degree (23.5%) of resistance was observed in this study. Various other studies have also reported an increased resistance of *Nocardia* species to drugs containing sulfonamide [7,9,19].

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Conflict of interests: No conflict of interests is declared.