

## Short communication

# Clinical pattern of nocardiosis in Saudi Arabia: a case series

A.M. Hakawi<sup>1</sup> and F.A. Al Rabiah<sup>2</sup>

النمط السريري لداء النوكارديا في المملكة العربية السعودية: سلسلة حالات  
أحمد محمد حقوي، فهد عبد العزيز الربيع

**الخلاصة:** استهدف الباحثان دراسة هذه الأنماط السريرية لداء النوكارديا في إحدى مستشفيات الرعاية الثالثة (التخصصية) في المملكة العربية السعودية، مستخدمين في ذلك مراجعة استيعابية للحالات في المدة بين 1987 و2003، وقد اكتشفا 19 حالة ثبتت بالزرع إصابتها بعدوى النوكارديا. وقد كانت الحالة المستتبنة الأكثر شيوعاً هي زراعة الكلية في 8 مرضى (42%). وكانت الرئتان هما أكثر مواقع الإصابة شيوعاً (12 مريضاً يشكلون 63% من الحالات). وقد استفردت ثلاثة أنواع من النوكارديا لدى هؤلاء المرضى، وهي النوكارديا النجمية (58%)، والنوكارديا البرازيلية (21%) والنوكارديا الملتهبة لأذن القبيعة (21%). ويتطلب تشخيص المرض رفع منسوب الاشتباه بالمرض لدى المرضى الذين لديهم استعداد للإصابة به، والذين يراجعون لإصابتهم بارتشاحات رئوية أو بخرجات دماغية أو بخرجات الأنسجة الرخوة العميقة، كما يتطلب التشخيص أيضاً متابعة دؤوبة وفعالة للإجراءات التشخيصية مع إعطاء المعالجة الملائمة في وقت مبكر.

**ABSTRACT** We aimed to study the clinical pattern of nocardiosis in a tertiary care hospital in Saudi Arabia using a retrospective review of cases from 1987 to 2003. A total of 19 patients were identified as having culture-proven nocardial infection. The most common underlying condition was renal transplantation in 8 patients (42%). Lungs were the most common sites of involvement in 12 patients (63%). Three *Nocardia* species were isolated in our series: *N. asteroides* (58%), *N. brasiliensis* (21%), and *N. otitidiscaviarum* (21%). A high index of suspicion is essential in susceptible patients presenting with pulmonary infiltrate, cerebral abscess or deep soft-tissue abscess and usually requires an active diagnostic workup and early administration of appropriate therapy.

## Tableau clinique de la nocardiose en Arabie saoudite : série de cas

**RÉSUMÉ** Notre objectif était d'étudier le tableau clinique de la nocardiose dans un hôpital de soins tertiaires d'Arabie saoudite grâce à une analyse rétrospective des cas entre 1987 et 2003. Au total, on a établi que 19 sujets étaient atteints d'une infection à *Nocardia* confirmée par culture. L'antécédent le plus fréquent était une transplantation rénale, chez 8 patients (42 %). L'atteinte pulmonaire, chez 12 patients (63 %), représentait la localisation la plus courante. Trois espèces de *Nocardia* ont été isolées dans la série concernée : il s'agit de *N. asteroides* (58 %), *N. brasiliensis* (21 %) et *N. otitidiscaviarum* (21 %). Un indice de suspicion élevé est déterminant chez les sujets vulnérables présentant un infiltrat pulmonaire, un abcès cérébral ou un abcès profond des tissus mous et nécessite généralement une démarche active de diagnostic ainsi que l'administration rapide d'un traitement approprié.

<sup>1</sup>Section of Infectious Diseases, Department of Medicine, King Fahad Medical City, Riyadh, Saudi Arabia (Correspondence to A. Hakawi: ahakawi@yahoo.com).

<sup>2</sup>Section of Infectious Diseases, Department of Medicine, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia.

Received: 12/02/06; accepted: 12/04/06

## Introduction

*Nocardia* spp. are aerobic, branching, partially acid-fast actinomycetes that inhabit the soil [1]. The majority of cases in humans are acquired through inhalation or direct skin inoculation [2]. No human-to-human transmission has been documented so far [3]. Nocardiosis is usually an opportunistic infection and most commonly presents as pulmonary disease. Clinical diagnosis is difficult as the symptoms and signs are not as specific as the radiological findings. Techniques for serological diagnosis are unreliable and unavailable commercially in most of the world [1], thus evaluation of appropriate specimens by smear and culture remains the principal method of diagnosis. If *Nocardia* spp. are isolated from normally sterile sites there can be a strong suspicion of the organism's role as an etiologic agent [2].

We have retrospectively reviewed 19 patients with nocardiosis in a tertiary care centre in Saudi Arabia, which represents, to our knowledge, the largest series of patients with nocardiosis reported from the Eastern Mediterranean Region.

## Methods

A retrospective chart review study of patients diagnosed as having nocardiosis at King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia. The hospital is a 650-bed tertiary care centre serving patients from the whole of Saudi Arabia. The hospital is designed to manage patients with complex medical problems, including immunocompromised patients and organ transplant recipients. The study period was from 1987 to 2003. The medical records were complete for all the patients as our centre has a very well-established health information system. We

reviewed their clinical, microbiological, and radiological characteristics in addition to the types of treatment given. The cases of nocardiosis were identified from databases of the infectious diseases service and the microbiology laboratory. Cases of nocardiosis were defined as any case with culture-proven *Nocardia* spp. from a specimen obtained through an invasive procedure (e.g. bronchoalveolar lavage, deep-tissue biopsy, etc.).

## Results

A total of 19 patients were identified as having a culture-proven diagnosis of nocardiosis; 16 were male (84%) and 3 were female (16%). The mean age was 40.3 (standard deviation 12.2) years. Fever was the presenting complaint in 15 patients (79%), and leukocytosis (white blood cells  $> 12 \times 10^9$  cells/L) was present in 12 patients (63%).

Predisposing factors for developing nocardiosis were identified in 17 patients (89%). Renal allograft transplantation recipients constituted 42% of those patients, while underlying malignancies were found in 26% (Table 1). In 2 patients of our series (11%), there was no clear risk factor identified. There were no data suggesting a nosocomial origin for the pathogens as all the patients came from the community. The most common site of involvement was the lung in 12 patients (63%), followed by the skin in 3 patients (16%). Other sites of involvement were the brain in 2 patients (11%) and joints in 2 patients (11%).

Invasive procedures are often needed to reach the diagnosis of nocardiosis. Among the 12 patients with pulmonary nocardiosis, bronchoscopy and bronchoalveolar lavage were carried out for 9 patients (75%), while the other 3 underwent open lung biopsy

**Table 1 Underlying conditions identified in patients with nocardiosis (n = 19)**

Underlying conditions	No.	%
Renal transplantation	8	42
Liver transplantation	1	5
Bone marrow transplantation	1	5
Leukaemia	2	11
Lymphoma	1	5
Other malignancies	2	11
Chronic steroid use	2	11
Unknown	2	11

to reach the diagnosis. The most common radiological pattern noticed in pulmonary nocardiosis was bilateral airspace consolidation found in 10 out of 12 patients (83%) with pulmonary nocardiosis. Other radiological patterns seen in our patients include a solitary lung nodule in 1 patient and a cavitary lung lesion in 1 patient. Brain biopsy was essential to diagnose cerebral involvement in the 2 patients with intracranial nocardiosis. At the same time, skin biopsy and joint aspiration were needed to diagnose nocardiosis in patients presenting with septic arthritis and skin abscess.

The most common species was *N. asteroides*, which was isolated from 11 patients (58%). Other species isolated in our series included *N. brasiliensis* in 4 patients (21%) and *N. otitidiscaviarum* (formerly *N. caviae*) in 4 patients (21%) (Table 2).

Unfortunately sensitivity testing was not available for most of the isolates.

Trimethoprim-sulfamethoxazole (TMP-SMX) was the first line of therapy for 12 patients (64%), and was used in combination with other antibiotics in 5 patients (26%). There were only 2 patients who received a course of antibiotics not including TMP-SMX. These were imipenem, amikacin, and ceftriaxone. TMP-SMX was withdrawn from 4 patients (21%) who experienced side-effects attributed to this drug. These included hepatotoxicity in 2 patients, renal toxicity in 2 patients and severe nausea and vomiting in 1 patient. The duration of treatment ranged from 3 to 12 months. Both patients with brain nocardiosis underwent surgical drainage of the abscesses in addition to antibiotic therapy.

Outcome analysis was available for 15 patients (79%), as 4 patients (21%) did not attend for follow-up visits. There were 11 patients (58%) who had documented clinical, microbiological and radiological cure of the illness and 4 patients (21%) who died during hospitalization (all with pulmonary nocardiosis) because of the concomitant bacterial pneumonia complicated by septic shock leading to death in the intensive care unit.

## Discussion

Infections caused by *Nocardia* spp. are infrequent, but challenging to clinicians.

**Table 2 Isolates of *Nocardia* spp. and their sites of involvement (n = 19)**

<i>Nocardia</i> spp.	Total		Site of involvement			
	No.	%	Lung No.	Brain No.	Skin No.	Joints No.
<i>Nocardia asteroides</i>	11	58	9	2	0	0
<i>Nocardia brasiliensis</i>	4	21	3	0	1	0
<i>Nocardia otitidiscaviarum</i>	4	21	0	0	1	3

In recent years, the number of case reports has been increasing, and this could be attributed to improvements in diagnostic capabilities and the increased prevalence of immunocompromised patients. In our series, most of the nocardial infections occurred in patients with suppressed immunity, especially organ transplant recipients. Chronic use of corticosteroids is a major predisposing factor for pulmonary nocardiosis [4]. Immunocompetent people could develop nocardial infections, as shown in our series and in previous reports as well [5]. The mean time to develop nocardiosis in renal transplant recipients was 18 months from the time of transplantation, and this is compatible with what had been reported previously [6,7]. Although there is an emerging problem of nocardial infection among patients with human immunodeficiency virus (HIV) [8], this was not noticed in our series, as all patients were HIV-negative.

Pulmonary nocardiosis, which is the most common disease entity in our series, usually presents with productive cough with no specific sputum colour. The radiological pattern commonly seen in those patients is bilateral airspace consolidation and this is consistent with other reports [4,9–11]. Extrapulmonary dissemination was not detected in any of our patients with pulmonary nocardiosis, although previous estimates suggest it is seen in 10%–15% of cases [9,12–14].

Patients with brain abscess due to *Nocardia* spp. usually present with fever, seizures and focal neurological signs. The radiological pattern of *Nocardia*-associated brain abscesses shows them to be variable in location and number [15,16]. They can occur at any site of the brain with single or multiple lesions. Both of our patients had parietal lobe involvement with a single lesion. The treatment of brain nocardiosis

should include a combined medical and surgical approach [16–18].

Septic arthritis due to *Nocardia* spp. is a rare clinical entity. Synovial fluid cultures are required to make the diagnosis. The synovial fluid analysis usually reveals an inflammatory pattern of cells with predominant polymorphonuclear leucocytes. These findings were shown in our patients and in previous patients reported in the literature [19–21]. Treatment with TMP–SMX for a minimum of 6 months is adequate [21,22].

Subcutaneous nocardial infection is a rare disease which tends to follow dissemination from other parts of the body [23–26]. Interestingly, all 3 patients with nocardial skin abscess in our series were found to have primary skin infections with no evidence of involvement of other sites. Similar cases were reported by other investigators [27–29].

Sulfa-containing antimicrobials remain the drugs of choice for nocardiosis. They have been proven to improve survival when used alone or in combination with other antimicrobials [30,31]. Primary agents that have been used successfully in treatment of nocardiosis include minocycline, amikacin, ceftriaxone, imipenem and linezolid [18,31,32]. Combining one or more of these agents with sulfa-containing antimicrobials has been recommended for serious systemic infections. Other potentially efficacious choices include amoxicillin–clavulanate, the new macrolides and the fluoroquinolones [33–37]. The duration of therapy is uncertain, but it should be at least 3 to 6 months. In some cases, such as central nervous system involvement, the duration of treatment could be extended to 12 months [18,30].

The outcome for patients with nocardiosis is favourable for those who are diagnosed early and receive adequate treatment. The

cause of death in nocardiosis patients is attributed to concomitant bacterial infections that are prevalent in the type of patients who are prone to nocardiosis.

In conclusion, our case series confirms that there is no clinical syndrome that is

pathognomonic for nocardiosis. A high index of suspicion is essential in susceptible patients presenting with pulmonary infiltrate, cerebral abscess, or deep soft tissue abscess, and usually requires an active diagnosis workup and early administration of appropriate therapy.

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