Nocardiosis at an Organ Transplant Center in Saudi Arabia: 15 years’ experience

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Abstract

Background: Nocardiosis is a rare infection that affects immunocompromised patients on immunosuppressive medications used for transplantation and cancer therapy. Such therapies are becoming more widely available in the Middle East region. Yet, reports on nocardiosis are scarce. Materials and Methods: This was a retrospective analysis of patients who were diagnosed with nocardiosis from 2004 to 2018 at a transplantation and cancer center. Nocardiosis were defined per the European Organization for Research and Treatment of Cancer criteria. Results: During the study period, 35 patients with nocardiosis (male: 68.5%) were identified. The most common underlying associated condition was transplantation 11 (31.4%), followed by malignancy 7 (20%), connective tissue disease and sarcoidosis 7 (20%), chronic lung disease 5 (14%), miscellaneous conditions 4 (11%), and one patient with human immunodeficiency virus. Nocardia was disseminated in 8 patients (22.9%) and isolated in 27 (77.1%); the latter included 13 patients (37.1%) with bronchial form, 11 (31.4%) with isolated visceral form, and 3 (8.6%) with cutaneous form. Pulmonary involvement occurred in 90% of the cases with cough, fever, and dyspnea being the most common symptoms. The main strain isolate was Nocardia asteroides, and the cure rate was 90%. Mortality related to nocardiosis occurred in 3 transplant patients (8.6%). Conclusion: Wider use of immunosuppressive therapy warrants vigilance to nocardiosis, which can present in a myriad of clinical forms. In our series, mortality was confined to the transplantation group, probably because of the relatively heavy immunosuppression. Nonetheless, prognosis is favorable if the infection is recognized and treated early.

Keywords: Bone marrow transplant, corticosteroids, immunocompromised host, immunosuppressive therapy, Nocardia, solid organ transplant

INTRODUCTION

Nocardiosis is a rare Gram-positive bacterial infection caused by aerobic actinomycetes in the genus Nocardia. Taxonomy of Nocardia has been revised and expanded based on the evolving molecular characterization and antimicrobial drug susceptibilities; Nocardia asteroides was, therefore, subsequently named as N. asteroides complex, which includes many subtypes.[1,2] The genus Nocardia is usually an “opportunistic pathogen” that classically causes infections in immunocompromised patients. Both solid organ transplant (SOT) and bone marrow transplant (BMT) are major risk factors for nocardiosis; graft rejection and immunosuppressive therapy are additional risk factors in those groups.[3-8] Other risk factors include malignancy, immune disease, diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), and human immunodeficiency virus (HIV) infection.[9-12]
Materials and Methods

This was a retrospective study that was conducted at King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia, which is a large tertiary care referral hospital with a bed capacity of over 1200. A search was done for all cases in whom Nocardia was isolated by modified acid-fast bacillus stain and cultures of all clinical specimens in the microbiology laboratory database during the period (January 1, 2004–December 31, 2018). The patients’ medical charts were reviewed, and the following information was obtained: sex, age, causes of immunocompromised status including organ transplantation, immunosuppressive therapy, malignancy, immune deficiency disorders, HIV infection, associated comorbidities, concomitant opportunistic infection and acute rejection for organ-transplanted patients, clinical presentations, laboratory results, microbiological cultures, radiological assessment, treatments, and outcome of the patients.

Definitions

In this study, we included all patients in whom Nocardia was isolated from clinical specimens. Pulmonary nocardiosis was classified to a proven or probable pulmonary Nocardia (PN) infection according to the European Organization for Research and Treatment of Cancer criteria for invasive aspergillosis[19] patients had to fulfill one of the following conditions for study entry:

1. Proven PN: A positive culture from samples taken from a sterile primary site, for example, pleural effusion, blood, cerebrospinal fluid, tissue biopsy, or abscess puncture AND (i) radiological findings on chest X-ray or computerized tomography (CT) scan of the thorax compatible with pulmonary nocardiosis OR (ii) clinical signs and symptoms of a lower respiratory tract infection (cough, sputum, dyspnea, and fever >38.3°C).

2. Probable PN (one of the following): (i) a positive culture from sputum, tracheobronchial aspirate, or bronchoalveolar lavage AND (a) clinical signs and symptoms of a lower respiratory tract infection (cough, sputum, dyspnea, and fever >38.3°C) AND (b) radiological findings on chest X-ray or CT scan of the thorax consistent with pulmonary nocardiosis; (ii) microscopic proof of Gram-positive, branching, partially acid-fast filamentary bacteria in histological samples (identified as Nocardia spp.) AND (a) clinical signs and symptoms of a lower respiratory tract infection (cough, sputum, dyspnea, and fever >38.3°C) OR (b) radiological findings on chest X-ray or CT scan of the thorax consistent with pulmonary nocardiosis.

Results

A total of 35 cases of nocardiosis were identified during the period, with a range of follow-up of 12-156 months and a mean of 71 months. Nineteen patients were proven PN (54%), 13 patients were probable PN (37%), and 3 patients with cutaneous nocardiosis (9%).

Patient characteristics and underlying conditions

Table 1 summarizes the demographic and clinical characteristics of the patients, and Table 2 shows some of these features according to the clinical group. The age range of our studied patients was 5 and 80 years (median: 58 years). The majority were males (68.5%).

At diagnosis, 20 patients (57.1%) have been receiving immunosuppressant medications for more than 3 months (steroids, CNI, mycophenolate moftel or infliximab, antimetabolites, and a number of chemotherapeutic agents). Most were receiving combinations of these drugs (13 [37%] patients), while 7 patients (20%) only were on monotherapy. Three patients (8.5%) finished courses of chemotherapy shortly before the diagnosis of nocardiosis. Steroids were the most utilized immunosuppressive drug (15 of 20 patients) [Table 1].

A history of bone marrow or organ transplant was the most common associated, as outlined in Table 1. The mean interval between the
transplantation and diagnosis of the infection was 9 months (range of 1.5–24 months); for the BMT group, the mean was 15 months, while for the SOT, it was 3.45 months. All organ transplant patients were receiving different combinations of immunosuppressive agents except a child diagnosed with severe combined immunodeficiency disease RAG2 gene mutation. An episode of acute rejection was reported in 5 patients (14.2%) before the diagnosis of nocardiosis. Five patients (14.2%) were diagnosed with cytomegalovirus (CMV) with or without other opportunistic infections and were on treatments including acyclovir, antifungals, and doxycycline. Only one patient was receiving trimethoprim-sulfamethoxazole (TMP-SMX) prophylaxis at diagnosis.

A history of malignancy was observed in 7 (20%) patients [Tables 1 and 2]. No one at diagnosis was on TMP-SMX prophylaxis or on treatments for other infections. Different disorders with derangement in the immune system including connective tissue disease and sarcoidosis were observed in 7 (20%) patients [Tables 1 and 2]. All were on single immunosuppressive therapy except one case with sarcoidosis. At diagnosis of nocardiosis, only one patient was on TMP-SMX prophylaxis.

Other associations included chronic lung disease, which was observed in 5 patients (14.2%). Of those, 3 patients had COPD; one of them had associated bronchiectasis, another had severe emphysema and was on chronic steroid therapy, and the last one had DM as well. The other 2 patients had interstitial lung disease, and they were on chronic steroid therapy.

There were three patients with DM but were otherwise immunocompetent. Two of them had cutaneous nocardiosis and responded to local medical treatment. The third patient suffered from stroke and sepsis and presented with pneumonia and pleural effusion. One immunocompetent patient had Madura foot and responded to TMP-SMX. Finally, HIV was diagnosed in one patient only (73 years old) on highly active antiretroviral therapy [Tables 1 and 2].

**Clinical and laboratory characteristics**

The isolated *Nocardia* form was found in 27 (77.1%) and

| Characteristic | n (%) |
|---------------|-------|
| Pain          | 3 (8.5) |
| Skin discharge| 3 (8.5) |
| Abscess formation | 1 (2.8) |
| Lymph node swelling | 1 (2.8) |
| CNS           | 1 (2.8) |
| Outcome       |       |
| Cure          | 27 (77.1) |
| Death         | 8 (22.8) |

BMT: Bone marrow transplant, CNI: Calcineurin inhibitor, CNS: Central nervous system, COPD: Chronic obstructive pulmonary disease, CT: Computerized tomography, DM: Diabetes mellitus, ILD: Interstitial lung disease, MRI: Magnetic resonance imaging, SCID: Severe combined immunodeficiency disease, S/P: Status post, TMP-SMX: Trimethoprim-sulfamethoxazole, HIV: Human immunodeficiency virus

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**Table 1: Clinical and demographic characteristics**

| Characteristic                                      | n (%) |
|----------------------------------------------------|-------|
| Gender                                             |       |
| Males                                              | 24 (68.5) |
| Underlying condition                               |       |
| Transplantation                                     | 11 (31.4) |
| BMT                                                | 6 (17.1) |
| Renal transplant                                    | 3 (8.5) |
| Liver transplant                                    | 1 (2.8) |
| Lung transplant                                     | 1 (2.8) |
| Malignancy                                          | 7 (20) |
| Squamous cell carcinoma                             | 2 (5.7) |
| The larynx prostate adenocarcinoma                  | 1 (2.8) |
| Hepatocellular carcinoma and large B-cell lymphoma  | 1 (2.8) |
| Non-Hodgkin lymphoma (S/P chemotherapy with no BMT) | 2 (5.7) |
| Acute myeloid leukemia                              | 1 (2.8) |
| Connective tissue disease and sarcoidosis           | 7 (20) |
| Sarcoïdosis                                         | 2 (5.7) |
| Rheumatoid arthritis                                | 1 (2.8) |
| Interleukin-12/interferon-gamma axis defect versus  | 1 (2.8) |
| subte T-cell dysfunction                            |       |
| Undifferentiated vasculitis                         | 1 (2.8) |
| ILD secondary to Sjogren syndrome                   | 1 (2.8) |
| Evans syndrome                                      | 1 (2.8) |
| Chronic lung disease                                | 5 (14.2) |
| COPD                                                | 2 (5.7) |
| Bronchiectasis                                      | 1 (2.8) |
| ILD (idiopathic)                                    | 2 (5.7) |
| HIV                                                 | 1 (2.8) |
| Other chronic medical disorders                     | 4 (11.4) |
| Diabetes mellitus                                   | 3 (8.5) |
| Cardiovascular disorder                             | 2 (5.7) |
| Madura foot                                         | 1 (2.8) |
| Morbid obesity                                      | 1 (2.8) |
| Stroke                                              | 1 (2.8) |
| Colon diverticulosis                                | 1 (2.8) |
| Immunosuppressive treatment                         |       |
| Monotherapy                                         | 7 (20) |
| Corticosteroids                                     | 6 (17.1) |
| Mycophenolate mofetil                               | 1 (2.8) |
| Combination therapy                                 | 13 (37.1) |
| Steroids and CNI                                    | 6 (17.1) |
| Steroids and azathioprine                           | 2 (5.7) |
| Steroids, methotrexate, and infliximab              | 1 (2.8) |
| Chemotherapy and CNI                                | 1 (2.8) |
| Clinical forms                                      |       |
| Disseminated                                        | 8 (22.8) |
| Isolated                                            | 27 (77.1) |
| Isolated bronchial form                             | 13 (37.1) |
| Isolated visceral (pneumonic) form                  | 11 (31.4) |
| Isolated cutaneous form                             | 3 (8.5) |
| Clinical presentation                               |       |
| Cough                                               | 22 (62.8) |
| Fever                                               | 11 (31.4) |
| Dyspnea                                             | 8 (22.8) |

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**Table 1: Contd...**

| Characteristic | n (%) |
|----------------|-------|
| Pain           | 3 (8.5) |
| Skin discharge | 3 (8.5) |
| Abscess formation | 1 (2.8) |
| Lymph node swelling | 1 (2.8) |
| CNS            | 1 (2.8) |
| Outcome        |       |
| Cure           | 27 (77.1) |
| Death          | 8 (22.8) |

BMT: Bone marrow transplant, CNI: Calcineurin inhibitor, CNS: Central nervous system, COPD: Chronic obstructive pulmonary disease, CT: Computerized tomography, DM: Diabetes mellitus, ILD: Interstitial lung disease, MRI: Magnetic resonance imaging, SCID: Severe combined immunodeficiency disease, S/P: Status post, TMP-SMX: Trimethoprim-sulfamethoxazole, HIV: Human immunodeficiency virus

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*Contd...*
included 13 patients (37.1%) with the bronchial form, 11 patients (31.4%) with the isolated visceral form (in our series, all involved lung only [pneumonic]), and 3 patients (8.6%) with the cutaneous form. The disseminated form was diagnosed in 8 (22.9%) patients. The main symptoms were cough (60%), fever (31.4%), dyspnea (22.8%), and others, as shown in Tables 1 and 2. Laboratory tests showed leukocytosis in 22.8% of the patients and lymphopenia in 25.7% of the patients.

**Radiological characteristics**

Radiological assessment by chest radiography and CT was done for all patients with the exception of one immunocompetent patient with cutaneous lesion [Tables 2 and 3]. New radiological findings were recorded in 19 patients (54.2%); all patients with organ transplant (11) and 3 patients with malignancy had new radiological findings. None of the patients with bronchial form and chronic lung diseases had any new radiological findings.

**Microbiological characteristics**

*Nocardia* strains were isolated from the sputum of 28 patients (80%); isolated species and the type of clinical sample that yielded the growth are shown in Table 4. Six cases of *Nocardia asteroides* were further speciated by biochemical testing, and *Nocardia farcinica* was identified in 4 and *Nocardia cyriacigeorgica* in 2. Nucleic acid amplification assays were not performed.

**Treatment and outcome**

There were 8 documented deaths; 5 were due to progression of the primary disease and 3 were related directly to nocardiosis. All the nocardiosis-related mortalities occurred in the organ transplant patients with isolated pneumonic form [Tables 1 and 2]. Of the 27 patients (77.1%) with isolated forms, 20 (57.1%) recovered completely after antibiotic therapy [details are shown in Table 4]. Among 8 (22.8%) patients with disseminated form, 4 were treated with TMP-SMX only and all recovered. The

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**Table 2: Patients’ clinical presentation characteristics according to the clinical form of nocardiosis**

| Parameter             | General, n (%) | Disseminated 8 patients | Visceral 11 | Bronchial 13 | Cutaneous 3 |
|-----------------------|----------------|-------------------------|-------------|-------------|-------------|
| Mean age, years       | 52.25          | 33                      | 55          | 63          | 50          |
| Underlying conditions, n (%) | 35 (100) | 3 2 - - | 1   2 4 - | 1 5 - - | - 1 - - |
| SOT                   | 5 (14.2)       | 3 2 - - | - 3 4 - | - 5 - - | - 1 - - |
| BMT                   | 6 (17.1)       | 3 3 - - | 2 1 4 - | - - 5 - | - - 3 - |
| Malignancy            | 7 (20)         | - 3 4 - | 2 - 4 - | - - 5 - | - 1 - - |
| Immune disease        | 7 (20)         | 2 1 4 - | - - 5 - | - - - - | - - 3 - |
| Chronic lung disease  | 5 (14.2)       | - - 5 - | - - - - | - - 3 - | - - 5 - |
| Immunocompetent       | 4 (11.4)       | - 1 - - | - - - - | - 1 - - | - - 3 - |
| HIV                   | 1 (2.7)        | - 1 - - | - - - - | - - 3 - | - - 5 - |
| Immunosuppressive drugs | 20 (57.1) | 4 5 6 - | - - - - | - - - - | - - - - |
| Steroids              | 15 (42.8)      | 4 5 6 - | - - - - | - - - - | - - - - |
| Antimetabolites       | 3 (8.5)        | - 1 2 - | - - - - | - - - - | - - - - |
| Calcineurin inhibitors| 7 (20)         | 4 3 - - | - - - - | - - - - | - - - - |
| Chemotherapy          | 4 (12.5)       | 1 2 4 - | - - - - | - - - - | - - - - |
| Mycophenolate mofetil | 1 (2.8)        | 1 - - - | - - - - | - - - - | - - - - |
| Infliximab            | 1 (2.8)        | - - 1 - | - - - - | - - - - | - - - - |
| No treatment          | 15 (42.8)      | 2 4 6 - | - - - - | - - - - | - - - - |

| Symptoms              |          |          |          |          |          |
|-----------------------|----------|----------|----------|----------|----------|
| Cough                 | 22 (62.8)| 3 10 8 - | - - - - | - - - - | - - - - |
| Fever                 | 11 (31.4)| 5 6 - - | - - - - | - - - - | - - - - |
| Dyspnea               | 8 (22.8)| 2 2 4 - | - - - - | - - - - | - - - - |
| Pain                  | 3 (8.5)  | 3 - - - | - - - - | - - - - | - - - - |
| Skin discharge        | 3 (8.5)  | - - - - | - - - - | - - - - | - - - - |
| Abscess formation     | 1 (2.8)  | 1 - - - | - - - - | - - - - | - - - - |
| Lymph node swelling   | 1 (2.8)  | 1 - - - | - - - - | - - - - | - - - - |
| CNS manifestation     | 1 (2.8)  | 1 - - - | - - - - | - - - - | - - - - |

| Radiological characteristics |          |          |          |          |          |
|------------------------------|----------|----------|----------|----------|----------|
| New pulmonary infiltrates    | 19 (54.2)| 8 11 0 0 | - - - - | - - - - | - - - - |
| No new pulmonary infiltrates| 16 (45.7)| - - - - | 13 3 - - | - - - - | - - - - |

| Outcome, n (%)              |          |          |          |          |          |
|------------------------------|----------|----------|----------|----------|----------|
| Death due to nocardiosis    | 3 (8.5)  | 1 2 - - | - - - - | - - - - | - - - - |
| Death due to primary disease| 5 (14.2) | - 3 2 - | - - - - | - - - - | - - - - |
| Cure without sequela         | 27 (77.1)| 7 6 11 3 | - - - - | - - - - | - - - - |

SOT: Solid organ transplant, BMT: Bone marrow transplant, HIV: Human immunodeficiency virus, TMP-SMX: Trimethoprim-sulfamethoxazole
Nocardiosis is a rare disease that occurs primarily in immunocompromised patients, usually as a consequence of drugs, organ transplant, malignancy, immune disease, or infection. Immunosuppressive drugs are one of the major risk factors of nocardial infection, especially corticosteroids, which are used in the management of a wide range of medical conditions. In our study, most of the patients (57.1%) were on single or multiple immunosuppressive medications for over 3 months; corticosteroid therapy is the most common one. In addition, in our cohort, nocardiosis occurred mostly in the older age group, a finding that was noted previously, probably reflecting the declining immunity and multiple comorbidities. Finally, there was only one patient with HIV, reflecting the low prevalence in the region.

The underlying medical conditions determine the bacteriological spread and hence clinical picture of nocardiosis. In our cohort, organ transplant was the main underlying medical condition in nearly a third of the patients, and the proportion in previous studies ranged between 18.1%–44.1%. Such variation is probably explained by different referral patterns and patient populations. This high prevalence of nocardiosis in posttransplant patients is probably related to severe degree of immunosuppression related to therapy. Nearly half of our patients had episodes of acute rejection before the diagnosis of nocardiosis, another half had opportunistic infections, and all had CMV infections, and all nocardiosis-related deaths (3 patients) occurred in this group of patients.

All four different clinical forms were seen in our patients: an isolated pneumatic form, an isolated bronchial form, a disseminated form, and an isolated cutaneous form. Pulmonary involvement either as an isolated or disseminated form is very common in nocardiosis, and indeed, this was observed in over 90% of our patients. An underlying chronic lung disease was observed in all patients with the bronchial form but not in the patients with the isolated pneumatic form. In terms of symptoms, cough has been reported to be the most common among the respiratory symptoms, which was again noted in our series. Fever was observed in the isolated visceral pneumatic form, while the bronchial form was characterized by dyspnea. The disseminated form was observed in 22.8% of the patients, higher than figures previously reported in the literature (6%–13.5%). This might be attributed to the extensive use of the available radiological resources at our center that included full-body CT scanning and magnetic resonance imaging. In addition, many patients presented with multiple symptoms which may have alerted the treating physician to possible dissemination of the disease. The radiological findings in our patients were variable and nonspecific, with consolidation being the most common feature, which was reported in previous series, with the exception of a higher number of patients with mediastinal lymphadenopathy.

The isolated cutaneous form is usually observed in elderly patients with comorbidities. Three of our patients (two with the isolated cutaneous form and one with the bronchial form) only had DM, and one had Madura foot without any other comorbid medical condition or immunosuppressive therapy.

Table 3: Radiological characteristics*

| Radiological finding                  | n (%) |
|--------------------------------------|-------|
| New radiological infiltrates         | 19 (56) |
| No new radiological infiltrates (bronchial form) | 13 (38) |
| Normal (cutaneous form)              | 2 (5.9) |
| Lymph nodes                          | 19 (560) |
| Mediastinal                           | 4 (12) |
| Hilar                                 | 1 (2.9) |
| Parenchymal                           |       |
| Normal                                | 3 (8.8) |
| Abnormal                              |       |
| Reticulation                          | 6 (17.6) |
| Consolidation                         | 11 (32.3) |
| Ground glass                          | 6 (17.6) |
| Nodule                                | 5 (14.7) |
| Cavity                                | 3 (8.8) |
| Mass                                  | 1 (2.9) |
| Pleural effusion                      | 6 (17.6) |

*By chest radiography and computerized tomography of the chest (no. 34 patients)

Table 4: Microbiological characteristics and antibiotics

| Parameter             | n (%) |
|-----------------------|-------|
| Source of the diagnostic sample |       |
| Sputum                | 28 (80) |
| Blood culture         | 2 (5.7) |
| Tissue culture        | 2 (5.7) |
| Skin swabs            | 3 (8.5) |
| Isolated species      |       |
| Nocardia asteroides   | 28 (80) |
| Nocardia brasiliensis | 5 (14.2) |
| Nocardia otitidiscaviarum | 2 (5.7) |
| Treatment             |       |
| TMP-SMX alone         | 17 (48.5) |
| TMP-SMX with other antibiotics | 7 (20) |
| TMP-SMX and carbapenem | 2 (5.7) |
| TMP-SMX, imipenem, and amikacin | 3 (8.5) |
| TMP-SMX, amoxicillin/clavulanic acid, and levofloxacin | 1 (2.8) |
| TMP-SMX and itraconazole | 1 (2.8) |
| Other combinations    | 11 (31.4) |

TMP-SMX: Trimethoprim-sulfamethoxazole

other 4 were treated with combination therapy [Table 4]; 3 responded and one died due to progressive nocardiosis. There were no relapses in either group during the follow-up period.

Discussion

Nocardiosis is a rare disease that occurs primarily in immunocompromised patients, usually as a consequence of drugs, organ transplant, malignancy, immune disease, or infection. Immunosuppressive drugs are one of the major risk factors of nocardial infection, especially corticosteroids, which are used in the management of a wide range of medical conditions. In our study, most of the patients (57.1%) were on single or multiple immunosuppressive medications for over 3 months; corticosteroid therapy is the most common one. In addition, in our cohort, nocardiosis occurred mostly in the older age group, a finding that was noted previously, probably reflecting the declining immunity and multiple comorbidities. Finally, there was only one patient with HIV, reflecting the low prevalence in the region.

The underlying medical conditions determine the bacteriological spread and hence clinical picture of nocardiosis. In our cohort, organ transplant was the main underlying medical condition in nearly a third of the patients, and the proportion in previous studies ranged between 18.1%–44.1%. Such variation is probably explained by different referral patterns and patient populations. This high prevalence of nocardiosis in posttransplant patients is probably related to severe degree of immunosuppression related to therapy. Nearly half of our patients had episodes of acute rejection before the diagnosis of nocardiosis, another half had opportunistic infections, and all had CMV infections, and all nocardiosis-related deaths (3 patients) occurred in this group of patients.

All four different clinical forms were seen in our patients: an isolated pneumatic form, an isolated bronchial form, a disseminated form, and an isolated cutaneous form. Pulmonary involvement either as an isolated or disseminated form is very common in nocardiosis, and indeed, this was observed in over 90% of our patients. An underlying chronic lung disease was observed in all patients with the bronchial form but not in the patients with the isolated pneumatic form. In terms of symptoms, cough has been reported to be the most common among the respiratory symptoms, which was again noted in our series. Fever was observed in the isolated visceral pneumatic form, while the bronchial form was characterized by dyspnea. The disseminated form was observed in 22.8% of the patients, higher than figures previously reported in the literature (6%–13.5%). This might be attributed to the extensive use of the available radiological resources at our center that included full-body CT scanning and magnetic resonance imaging. In addition, many patients presented with multiple symptoms which may have alerted the treating physician to possible dissemination of the disease. The radiological findings in our patients were variable and nonspecific, with consolidation being the most common feature, which was reported in previous series, with the exception of a higher number of patients with mediastinal lymphadenopathy.

The isolated cutaneous form is usually observed in elderly patients with comorbidities. Three of our patients (two with the isolated cutaneous form and one with the bronchial form) only had DM, and one had Madura foot without any other comorbid medical condition or immunosuppressive therapy.
mortality rate in our study was 8.6% (3/35) which is lower than other reported studies[26] and may be related to early detection and treatment of the infection. There were five other mortalities due to the progression of the primary disease.

Limitations are bound to occur in this study because of its retrospective nature and the small number of patients. However, this was the case in nearly all previously reported series which had a similar number of patients or less basically because of the rarity of nocardiosis. Nonetheless, we believe that it is important to report this infection to emphasize vigilance, and surveillance, particularly among vulnerable groups.

**Conclusion**

Nocardiosis is a rare opportunistic infection in immunocompromised patients, including organ transplant recipients. Of note, all Nocardia-related mortalities occurred in this group of patients. A variety of clinical forms and the associated risk factors were observed in our study, with the isolated bronchial form being the most common. Prognosis and response to therapy is excellent if the infection is diagnosed and treated early. Because of the rarity of nocardiosis, multicenter collaborative prospective research on the epidemiologic, diagnostic, and therapeutic aspects of nocardiosis is warranted.

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**Conflicts of interest**

There are no conflicts of interest.

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Weheba, et al.: Nocardiosis at a transplant center