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Nocardia species infections in a large county hospital in Miami: 6 years experience

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Summary A review of all cases of nocardiosis in a large hospital in South Florida over the last 6 years was conducted. There were 25 cases of nocardiosis and 76% of them were also infected with HIV. Of the HIV infected patients, all of them had CD4 counts less than 100 cells/mm³ and most cases were localized in the lungs.

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Introduction

Nocardiosis is an uncommon, potentially severe disease caused by soil-borne actinomycetes, that usually affects immunocompromised hosts.¹ Nocardiosis presents as a localized or disseminated infection, most commonly introduced through the respiratory tract.² Traditionally, nocardiosis has been described in individuals receiving immunosuppressive therapy, organ transplant recipients, and patients with chronic pulmonary diseases. Since the advent of the HIV epidemic, there have been conflicting reports whether or not HIV infection has become one of the most common underlying conditions to predispose for nocardiosis.^{3,4} The objective of this study was to review the cases of *Nocardia* species infections in a large tertiary teaching hospital in South Florida over the last 6 years.

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Methods

A computerized database search was conducted to identify all patients with the diagnosis of nocardiosis at the time of discharge from Jackson Memorial Hospital from 01/01/1999 to 12/31/2004. A case report form was developed to abstract and collect information from the medical records of possible cases. Positive cases were defined if Nocardia species was isolated from a patient and the clinical course or presentation was consistent with an infection. Pulmonary disease was defined by the presence of positive cultures from a respiratory sample in addition to respiratory symptoms and/or radiographic infiltrates. Disseminated disease was defined by cultures of Nocardia from the blood stream or by the documentation of Nocardia infection in two or more organs of the body or the documentation of nocardiosis and presence of abnormal brain images (ring enhancing lesion in brain CT or MRI). For the analysis "current CD4 cell count" was considered to be the CD4 cell count available within 6 months of the diagnosis of nocardiosis. The underlying condition associated with

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nocardiosis was the one assessed by the primary team who managed the patient. Survival was assessed whether or not the patient survived the index hospitalization. Analysis of the data was done using descriptive statistics.

Results

Epidemiological features

We found 25 patients with *Nocardia* species infection in the studied period. The average age was 43 years (range 21–69, mean 44 years); 68% were men. Racial-ethnic distribution was as follows: African Americans, 48%; Haitians, 24%; Hispanics, 12%; and Caucasians, 12%. Seventy-six percent (19/25) of the population were also infected with HIV. In about a third of the HIV-related cases (7/19), both infections, nocardiosis and HIV infection, were found in the same hospital admission. CD4 cell count in the HIV-associated cases was available in 14 of the total of 19 patients. All CD4 cell counts were bellow 100 cells/mm³, and 85% (12/14) were bellow 50 cells/mm³. No patient was on antiretroviral therapy at the time of the nocardiosis diagnosis. Cases not associated with HIV infection (6/25) were associated with solid organ transplant (2), lung cancer (2), and severe pulmonary fibrosis (1).

Clinical features

Sites where the diagnosis of nocardiosis was made are shown in Table 1. In the majority of cases (21/25) the lungs were involved. In these cases, the sample was obtained by bronchoalveolar lavage or biopsy in nine cases and from sputum in 12 cases. There were nine cases (36%) of disseminated disease.

Radiographic studies

Computerized tomography (CT) of the chest or chest radiography (CXR) was available in 19 patients. CXR findings showed: mass with or without cavitation in nine cases; multilobar pneumonia in four; and localized infiltrate in three cases. CT findings were: infiltrate with cavitations, six cases; consolidation, six cases; and others three cases.

	Age/sex	HIV+	Risk factor	CD4 current	Culture sites	Location
1	45/M	Yes	Н	5	Lung (BAL)	Pulmonary
2	51/M	Yes	Н	15	Lung (BAL)	Disseminated: lung + brain
3	40/F	Yes	Н	10	Lung (sputum)	Pulmonar
4	49/M	Yes	Н	14	${\sf Neck}+{\sf mediastinal}$ abcesses	Disseminated: lung + neck + mediastinum
5	48/M	Yes	IVDA	0	R knee	Disseminated: lung + knee + mediastinum
6	40/M	Yes	IVDA	Not done	Lung (sputum)	Pulmonar
7	46/M	Yes	IVDA	Not done	Lung (biopsy)	Pulmonar
8	71/F	Yes		79	Lung (biopsy)	Pulmonar
9	54/M	Yes	Н	18	Lung (biopsy)	Pulmonar
10	48/M	Yes	IVDA	Not done	Lung (sputum)	Pulmonar
11	32/M	Yes	Н		Lung (sputum)	Pulmonar
12	35/M	Yes	Н		Index finger	Disseminated: lung + finger
13	45/M	Yes	Н	37	Lung (sputum) + arm	Disseminated: lung +
14	46/F	Yes	н	75		Pulmonar
15	27/M	Yes	Н	2	Blood culture	Disseminated: blood
16	31/F	Yes	Н	-	l ung (sputum) +	Disseminated: lung +
	• • • •			·	elbow/chest wound	elbow + chest wound
17	41/M	Yes	н	20	lung (sputum)	Pulmonar
18	37/M	Yes	MSM	32	Lung (sputum)	Pulmonar
19	30/F	Yes	Н	7	Lung (BAL)	Pulmonar
20	46/F	No		·	Lung (BAL)	Disseminated: lung + brain
21	67/M	No			Lung (sputum)	Pulmonar
22	26/M	No			Lung (sputum)	Pulmonar
23	44/F	No			Lung (biopsy)	Disseminated: lung + brain
24	57/M	No			Lung (BAL)	Pulmonar
25	42/F	No				Pulmonar

Neurologic involvement was sought in nine patients with computed tomography of the brain. It was abnormal in three cases. The radiographic appearance of the brain lesions was described as "ring enhancing lesions" and was called presumptive CNS nocardiosis since further confirmation was not obtained. Most patients were treated with sulfamethoxazole/trimethoprim.

Outcome

The total number of patients was 25. Of the total, 24 survived the index hospitalization. We found information regarding the outcome after discharge in eight of the 24 survivors. The outcomes were as follows: two expired 1 and 2 months later; the other 1 year later; three patients "improved" with followup appointments in the HIV clinic. Their improvement consisted of undetectable viral loads and raised CD4 cell counts; the remaining three survived for some time and then were lost to followup after they went to jail.

Discussion

Advanced HIV and nocardiosis

In the US, the studied period corresponds to several years after the widespread availability of both potent antiretroviral therapy and PCP prophylaxis. Despite this availability, HIV infection has become the most common underlying condition predisposing for nocardiosis.

We found 76% of our cases of nocardiosis have been associated with HIV infection in the period from 1999 to 2004. This study was done in Miami-Dade County where the AIDS case rate was 44.4 per 100,000 population in 2003.⁵ The most likely reason advanced HIV infection is becoming the leading predisposing factor for nocardiosis is this region's relatively high prevalence of HIV infection compared to other areas. Our patients did not have other known underlying immunosuppressive conditions present in addition to their HIV infection. However all patients who had HIV infection had profound immunosuppression.

In our series, all patients had a CD4 count below 100 cells/mm³, and 85% had a CD4 count below 50 cells/mm³. Whether or not the known HIV infected (12/19) patients were compliant with the sulfa-based PCP prophylaxis is not known. Four of these known cases were diagnosed with HIV infection within less than 1 year after the diagnosis of nocardiosis and it is possible these patients were not in HIV care and thus were not taking prophylactic medication. More importantly, nocardiosis was the initial manifestation of HIV infection in the other seven of the 19 cases associated with HIV.

These findings support the active search for HIV infection in all patients presenting with nocardiosis with no other obvious risk factor, in particular in areas of relatively high incidence of HIV infection.

Similarity of epidemiologic characteristics

The epidemiologic characteristics of patients with nocardiosis in this series tended to approximate the epidemiologic characteristics of HIV infection. Consistent with earlier reports, $^{4,6-8}$ we found that nocardiosis is more prevalent in males (68%). However this difference may be less dramatic if we consider that 70% of the adult AIDS cases in Florida in 2003 were males. By ethnic/racial breakdown: Blacks were 53% of the total adult AIDS cases in Florida in 2003, and represented 48% of our cases; Hispanics were 18% of the total adult cases in Florida, and 12% of our cases; Haitians represented approximately 15% of AIDS cases in Florida, 5,a and 24% of our cases.

The mode of transmission of HIV infection was documented in the records of 18 patients. Four of them (22%) were intravenous drug users, slightly higher than the 16% of cases of adult AIDS cases reported in Florida in 2003, but different from prior reports that ranged from 53% (in this institution)⁴ to 85%.⁶ It is unclear if this shift in the number of cases related to intravenous drug use may be related to the changing epidemiology of HIV infection or to other factors.

Overall clinical characteristics similar regardless of HIV status

The lungs were involved in the majority of the cases (21/25). This is similar to what has been described in the classic reports, ^{2,9,10} and most of the cases of disseminated disease also included the lungs.

CNS disease

CNS involvement is a well known complication of nocardiosis.¹¹ A large series reported a rate of about 20%. Presumptive CNS involvement was sought in nine cases with CT of the brain. There were three abnormal scans. Poorer prognosis is recognized in cases with CNS involvement. In this series, despite the limitation regarding outcome information due its retrospective nature, two of the three documented deaths occurred in patients with presumptive CNS involvement. In these cases there was extensive radiological involvement with minor or no symptoms. We believe this information supports the active search for possible CNS compromise in patients with documented nocardiosis.

Limitations

The main limitation of this report is related to its retrospective design. In many cases HIV testing was not sought because the patients had some other significant risk factors for immunosuppression. In patients with HIV infection full information was not always available, such as risk factors for HIV infection or current CD4 count. As mentioned above, outcome was only evaluated as survival at the end of the index hospitalization.

In most cases CNS involvement was not actively sought. However given the overall low incidence of nocardiosis a prospective study may be difficult to perform. Thus we

^a Haitians are not included as a separate ethnic/racial group in the Florida Annual report, and therefore are included in the percent of Blacks reported above.

think that despite the limitations of the present study, there is valuable information that can be obtained from it.

Conclusion

In South Florida, due to the high prevalence of HIV, the epidemiological characteristics of patients with nocardiosis resembled the HIV population as described above. The clinical characteristics of nocardiosis in HIV infected patients in this study were not distinctive compared to HIV negative patients.

Advanced HIV infection should be suspected in all cases of nocardiosis, in particular in subjects with no other apparent underlying condition and especially in areas with relatively high incidence of HIV infection.

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