

Clinical Experience With Pulmonary Nocardiosis In A Tertiary Care Hospital In Pakistan

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Research article

Keywords: Nocardiosis, Pulmonary nocardiosis, Pneumonia

Posted Date: June 5th, 2019

DOI: <https://doi.org/10.21203/rs.2.10125/v1>

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Abstract

Background Pulmonary nocardiosis is a rare disease. It usually affects immunocompromised patients. In this study we evaluated our clinical experience with pulmonary nocardiosis in our centre. Method It was a retrospective study done in Aga Khan University Hospital. Study was started after ethical approval. Cases from 2007 to 2017 were retrieved. Patient with diagnosis of Culture positive Pulmonary Nocardiosis with age more than 18 years included. Patient who were already on treatment of Nocardiosis at time of admission were excluded. Patients' medical records were reviewed to identify epidemiologic, clinical, microbiologic, and radiographic features. Data was entered on SPSS V22. Results 56 patient met inclusion criteria but 12 had missing data so 44 patients' data was included at end. 8 patients had disseminated disease. 52% were immunocompromised and 48% were immunocompetent. 31 were females. Diabetes mellitus was most common comorbidity. Fever and shortness of breath were most common presentations. Pleural effusion and consolidation were most common chest xray findings. Mean white cell count was $12.35 \pm 7 \times 10^9/L$. 70% patient had some degree of hyponatremia. Culture showed that all strains were sensitive to amikacin and 67% were sensitive to imipenem. Mean length of stay was 7.7days. 30 day mortality was 23%. 16% required ICU stay. There was significant difference between immunocompromized and immunocompetent group regarding 30 day mortality (p value 0.019) and ICU admission need (p value 0.021). Conclusion Pulmonary nocardiosis is often missed, high index of suspicion is required especially in immunocompromised patients and mortality is often very high.

Methods

This study was conducted in Aga Khan University Hospital in Pakistan. Retrospective data was collected from 2007 to 2017. ICD-9 code was used to identify all the cases with diagnosis of pulmonary nocardiosis during these 10 years. Patient with diagnosis of culture positive Pulmonary Nocardiosis with age more than 18 years were included. Patient who were already on treatment of Nocardiosis at time of admission were excluded.

Immunocompromised Patients were defined as

- Organ transplant Patients
- Active Solid or hematologic malignancy
- Patient on Immunosuppressive for last 3 months
- Patient who were on Prednisolone more than 10 mg or equivalent for more than 2 weeks at time of diagnosis⁸
- HIV patients
- Congenital immune deficiency patients

Nocardia infection at two or more noncontiguous sites and/or nocardemia was considered disseminated nocardiosis.

No identifiable data was recorded. Data was recorded on predefined questionnaire and included epidemiologic, clinical, microbiologic, and radiographic features. Culture data was obtained from Lab and sub species were reported as *Nocardia asteroides* or *Nocardia* other than *asteroides*. Data was entered in SPSS V22 for analysis. Mean and Standard deviation was calculated for Age, White blood cells (WBCs), C-Reactive protein (CRP), Serum electrolytes and total length of stay. Frequencies were calculated for qualitative data. Cross tabulation was done to find out significant variables for outcome. $P < 0.05$ was considered significant.

Results

56 patients met inclusion criteria but 12 of them had missing data on files review so were excluded. 44 patients' data was included for analysis. Among these, 8 had disseminated disease.

1. Demographics and comorbidities

Mean age of patients were 56 ± 16 years. 31 were Males and 13 were females. 32 % patient had diabetes mellitus while only one patient had HIV. Most common comorbidity was diabetes mellitus. 52% (23) were immunocompromised and 48 % (21) were immunocompetent patients. Long term steroid use was the most common cause of immune compromised status in our cohort, it was seen 48% of immunocompromised cases. 2nd most common reason of immunocompromised status was malignancies with 26% among immunocompromised cases. Rest of Comorbidities is shown in table 1.

2. Clinical features and laboratory data

83% patient had fever on presentation, while other presenting symptoms were Shortness of breath 41%, chest pain 9.3%, Hemoptysis 9%, cough 62%. On chest Xray, 11% had cavitating lesions, 48% had pleural effusion, 23% had consolidation and 12% were having normal chest xrays. Mean white cell count was $12.35 \pm 7 \times /L$, while 53% had normal white cell count. Mean serum sodium was 133 ± 6 mmol/l, while 70% patients' sodium was < 135 mmol/l. Rest of the blood count and biochemistry lab results are shown in table 2.

3. Microbiological Data

Microbiological data has shown that 54%(24patient) had *Nocardia asteroid* species on culture while 46% (20 patients) has non asteroid species. Our lab only reported results as *asteroides* and non *asteroides* species. All strains were sensitive to amikacin while imipenum sensitive strains were 67%. Least sensitive antibiotic was ciprofloxacin (12%). Details antibiotics sensitivities pattern is shown in Figure 1.

4. Outcome

Mean length of hospital stay was 7.7 ± 6 days. Sixteen percent (7 patients) needed ICU stay. 30 days mortality after diagnosis was 23%. On further subgrouping it was found out that 52% (23) were immunocompromised and 48 % (21) were immunocompetent patients and 30 days mortality was 36% in

immunocompromised and 10% in immunocompetent group. There further comparison is shown in table 3. There was significant difference between immunocompromised and immunocompetent group regarding 30 day mortality (p value 0.019) and ICU admission need (p value 0.021).

Discussion

Pulmonary nocardiosis is rare infection which may present both as primary disease and as opportunistic infection. Our study showed male preponderance, which is consistent with previous studies. The male predominance could be due to hormonal effects on virulence of *Nocardia*.^{9,10}

Pulmonary nocardiosis is regarded as to affect mostly with affected cellular immunity. In our study 48% of patient was immunocompetent and rest was immunocompromised. Most common cause of immune compromised state was long term steroid use 48%. Previous studies has shown immunocompromised hosts around 50-65%.¹¹ Diabetes mellitus was one of the common comorbidity that was found in our cohort. Poor control of diabetes can be one of the risk factor for having this disease as it was reported in previous cases reports.^{12,13}

None of our patient had bone marrow transplant (BMT). The risk of nocardiosis in BMT patient has decreased with the introduction of cyclosporine and trimethoprim/sulfamethoxazole (TMP-SMX) prophylaxis. In one centre, its rate was just 0.2%.¹⁴

The clinical recognition of nocardiosis is difficult as it has relatively low incidence and a lack of pathognomonic symptoms. A high index of clinical suspicion needs to be exercised to diagnose pulmonary nocardiosis. There has been some differences in presentation among immunocompromised and immunocompetent hosts. Like pleural effusion was most common presentation in immunocompromised hosts while immunocompetent hosts have consolidation as most common xray finding. In previous case series, common finding in immunocompetent hosts were nodules and opacities.¹⁵

Disease in immunocompromised host is slightly more severe than in immunocompetent hosts as they were found to be having more ICU admissions, more prolonged hospital stay and increased 30 days mortality. Microbiological data showed that there was mixed pattern of resistance. All strains were sensitive to amikacin while 1/3rd was resistance to trimethoprim and imipenem. Therefore, it is always important to get final sensitivities when treating these infections. Most active agents in our study were linezolid and amikacin. A study in Spain also looked into resistance pattern. Almost same resistance pattern was seen in their study.¹⁶

Limitation of this study are its being retrospective and we don't have PCR data to further classify *Nocardia* subspecies to see their differences. Regarding resistance pattern, we did not collect Minimum inhibitory concentration data (MIC) from our lab.

Conclusions

Pulmonary nocardiosis diagnosis is often missed resulting in delay in diagnosis and treatment. High index of suspicion is required in diagnosis of pulmonary nocardiosis especially in patients with underlying lung disease, immunocompromised status and long term steroid use. Despite treatment mortality remains high.

Abbreviations

BMT	Bone marrow transplant
CRP	C Reactive protein
HIV	Human immunodeficiency virus
ICD	International Disease classifications
ICU	Intensive care unit
MIC	Minimum inhibitory concentration
TMP-SMX	Trimethoprim and Sulfamethoxazole

Declarations

- **Ethics approval**

Ethical approval was taken from hospital ethics committee of Aga Khan University hospital.

- **Consent for publication**

Not applicable

- **Availability of data**

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request

- **Competing interest**

The authors declare that they have no competing interests.

- **Funding**

No funding

- **Authors contributions**

HA conceived of the study and drafted manuscript and helped in data analysis. KA collected and analysed data and helped in manuscript drafting. All authors read and approved and the final manuscript

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Tables

Table 1

Comorbidities

Condition	Percentage
DM	32
HIV	2
Malignancies	11
Asthma	20
Bone Marrow Transplants	2
Systemic Lupus Erythematosis	14
Cushing Syndrome	4
Interstitial Lung Disease	11
Chronic Kidney Disease	27

Table 2

Blood and Biochemistry panel

Lab test	Results
Hemoglobin	108±2 g/l
White blood cells	12.35±7×/L
Neutrophils	10.25±0.9×/L
Lymphocytes	1.25±0.5×/L
C-Reactive Protein	14±8.1 mg/l
Serum Sodium	133±6 mmol/l
Serum Potassium	3.9±0.8 mmol/l

Table 3

Comparison of Immunocompromized and immunocompetent patients

Variable	Immunocompromised (N =23)	Immunocompetent (N=21)	p Value
Age	49±17	59±14	
Most common presentation	Fever	Fever	
Most Common Chest Xray Finding	Pleural Effusion	Consolidation	
Disseminated Disease	9%	25%	0.101
Nocardia Asteroides	40%	58%	0.169
White cell count	10±6×/L	14.5±7×/L	0.033
C-Reactive Protein	16.3±8 mg/l	12.1±7 mg/l	0.152
Serum Sodium	132±6 mmol/l	133±5.7 mmol/l	0.569
Serum Potassium	3.8±0.7 mmol/l	4.06±0.8 mmol/l	0.452
Length of Stay	9.18±6 days	6.19±6 days	0.108
ICU admission	22%	9%	0.021
30 day Mortality	36%	10%	0.019

Figures

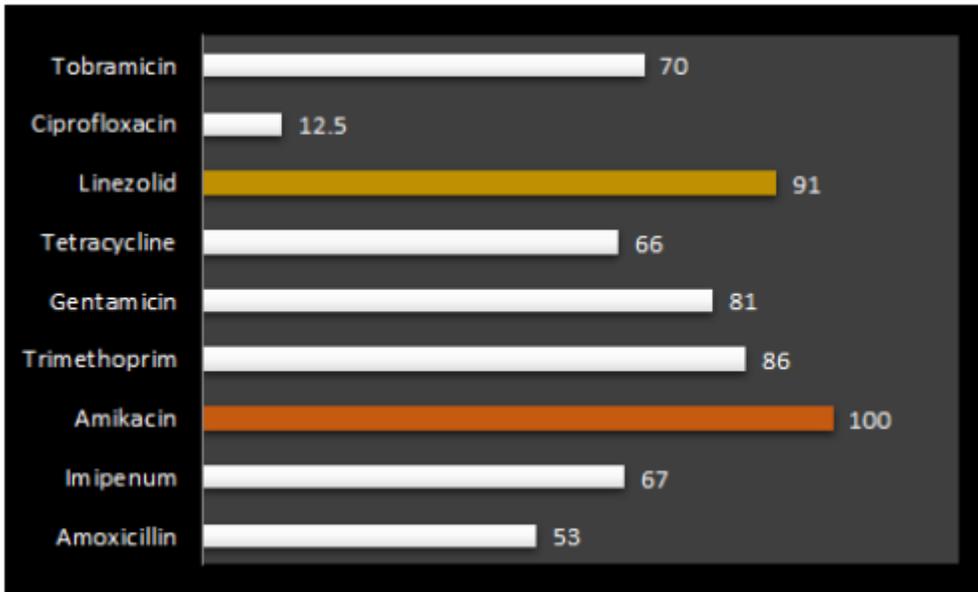


Figure 1

Nocardia antibiotics susceptibilities (Percentage)