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## Case Report

# A case report: *Nocardia otitidiscaviarum* bacteraemia in a patient with metastatic lung adenocarcinoma

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### ABSTRACT

A 73 years old male patient, was admitted with fever, cough and generalised weakness since two to three days. He was diagnosed to have metastatic adenocarcinoma of lung 3 months back and was on chemotherapy. His blood culture grew *Nocardia otitidiscaviarum*. The patient succumbed to the disease and various other comorbidities that had led to multi-organ failure. Incidence of bacteraemia due to nocardia and the associated common species in India is not known yet. It is imperative to widen the scope of the laboratory and to use diverse laboratory tools for accurate and rapid diagnosis of rare and unconventional pathogens.

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## 1. Introduction

*Nocardia* species are aerobic, partially acid-fast, branching gram-positive bacilli which produces colonies that produce aerial hyphae over 2 to 5 days. They are ubiquitous in environment. Nocardiosis and bacteraemia due to nocardia usually are seen among patients with solid organ transplantation (SOT), hematopoietic stem cell transplantation (HSCT), haematological malignancy, solid organ malignancy (SOM), Human immunodeficiency virus (HIV) infection, those receiving long-term corticosteroid therapy or other medications that suppress cell-mediated immunity, diabetes, and alcoholism.<sup>1,2</sup> As the patients with these risk factors increase in health care facilities globally, the risk of nocardiosis and bacteraemia due to nocardia increase; and it is imperative that the clinical suspicion and laboratory methods need to be improved too for detection, identification and antimicrobial susceptibility testing.

## 2. Case Report

A 73 years old male patient, was admitted with fever, cough and generalised weakness since two to three days in June 2022 in a tertiary care hospital in Mumbai, India. He had maculopapular rash on face, head and upper trunk since two days. The family gave the history of minimal response to verbal command since one day.

He was diagnosed to have metastatic adenocarcinoma of lung 3 months back. There was 2.5 cm mass in right lung along with involvement of mediastinal lymph nodes and vertebral bone lesions as seen on PET scan. Lung cancer panel after biopsy showed EGFR Exon 21 mutation positive And PDL-1: TPS: <1%. He was initiated with chemotherapy with Inj. Pemetrexed and Inj. Carboplatin. He had undergone 3 cycles of the chemotherapy. Other supportive management were provided to him as per chemotherapy protocol. He also was on treatment for arrhythmia for 2 years. He was admitted in the hospital for further management as his general condition was poor. He was clinically diagnosed to have varicella zoster infection.

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On admission, he was in metabolic acidosis. His important investigations were as mentioned. WBC count: 61,690/cmm with neutrophilia, Procalcitonin: 20.75ng/dl, CRP (C Reactive protein): 29.74mg/L, BUN (Blood Urea Nitrogen): 30.3 mg/dL, S.Creatinin 3.4 mg/dL, HbA1C: 7.9 (Average Sugar: 180mg /dL), AST (Aspartate Aminotransferase): 3985 U/L, ALT (Alanine Aminotransferase): 2365 U/L, Direct Bilirubin: 0.52mg/dL, Activated Partial Thromboplastin Time (APTT): 38.4Seconds, S.Na<sup>+</sup>: 131 mmol/L, S.Cl<sup>-</sup> : 95.5 mmol/L, CPK (Creatine Phosphokinase): 372 U/L, SARS-CoV 2 PCR: Negative, HIV Antigen and antibody detection test: Non-Reactive. ECG showed atrial fibrillation. Paired blood cultures were sent (Biomerieux, France).

Patient was treated with Inj. Gancyclovir, Piperacillin Tazobactam, supportive management for uncontrolled diabetes, deranged renal function test, and i.v. fluid as required. He also needed noninvasive ventilation support. Over the next two days, patient's general conditions deteriorated further. The patient was shifted to intensive care unit. Ionotropes were started. Patient was intubated for ventilator support. Escalation to meropenem was done. However, patient did not improve and on the fourth day of admission, he went into cardiac asystole. Cardiopulmonary resuscitation was initiated but the patient succumbed to the disease and various other comorbidities that had led to multi-organ failure.

Blood cultures flagged positive after 3 days of incubation. Gram stain of the flagged bottle showed filamentous branching gram positive bacilli which were acid fast with modified Zeihl Neelsen Stain. After 2 days of incubation whitish dry colonies grown on 5% sheep blood agar were identified as *Nocardia otitidiscaviarum* by Vitek MS (MALDI ToF, Biomerieux, France).

### 3. Discussion

India is a tropical country and presence of *Nocardia* in environment, in both, open spaces and at construction site is common. Our patient had community acquired nocardiosis. His Lung adenocarcinoma, chemotherapy and uncontrolled diabetes probably led to compromised local and systemic immunity which put him at risk of nocardiosis.

A study done over 2 decades revealed an increase in the annual incidence of *Nocardia* infection/colonization from 0.33 (1997–1998) to 0.87 (2007–2008) per 100,000 inhabitants ( $p = 0.001$ ). The past 2 decades have seen significant developments in both host and microbiological factors that has affected the epidemiology and incidence.<sup>3</sup> A study on nocardiosis in a tertiary care hospital in Chandigarh reported 12 consecutive cases over a span of 26 months which is higher than previous years.<sup>4</sup> Another study by Dawar et al., reported twelve cases of nocardiosis out of 32 clinically suspected cases. Eight of these patients were immunocompromised with the

history of organ transplantation, use of immunosuppressive agents or steroids.<sup>5</sup> Lungs remain the commonest primary site of infection of *Nocardia* and haematogenous spread occurs most cases with involvement of other organs like brain. Even though nocardia is known to spread through haematogenous spread, growing nocardia from blood still remains rare.<sup>1</sup> Several single-centre studies of patients with nocardiosis in the context of malignancy or Solid Organ Transplant (SOT), reported rates of nocardia bacteraemia are between 9–12%.<sup>6–8</sup> Single-centre studies of nocardiosis in HSCT (haemopoietic stem cell transplant) recipients have demonstrated higher proportions of patients with *Nocardia* bacteraemia (27–33%); however this is still significantly less than the 47–83% reported to have clinically disseminated disease.<sup>9–11</sup>

A case series from Australia reported four cases of nocardia in blood among immunosuppressed patients.<sup>12</sup> They also reviewed 277 cases of bacteraemia globally. 90% of these patients were immunosuppressed, solid organ malignancy contributing to 20% of the total of *Nocardia* bacteraemia.<sup>12</sup> Wang et al. reported 132 patients during 2002–2012 in the USA.<sup>8</sup> Identification of *Nocardia* in blood culture as single agent or as a coinfective organism hence should not be regarded it as a contaminant especially among immunosuppressed patients.<sup>13</sup> In a study of 17 cancer patients, bacteraemia was attributed to the catheter in 10 cases; for the other 7, it was a disseminated *Nocardia* infection.<sup>14</sup> Central venous catheters (CVC) are important for patients with cancer as *Nocardia* can form biofilms. Biofilm can be instrumental in causing as *Nocardia* bacteraemia in 59% of cancer patients.<sup>11</sup> Various species of nocardia causing bacteremia is reported.<sup>8,11–16</sup>

Singh et al. also had also found that diabetes mellitus contributed to 27.8% of the underlying risk factors for Nocardiosis.<sup>17</sup> In study done in Uttarakhand India, diabetes was found to be the most common risk factor for nocardiosis and consisted of 50% of cases followed.<sup>18</sup> Our patient had uncontrolled diabetes and malignancy both by COPD and lung malignancy. Also, chemotherapy could have decreased cell mediated immunity further adding to the problem.

A series from an Indian hospital demonstrated that 32 had Nocardiosis out of 860 patients with tuberculosis who had been treated previously with anti-tubercular drugs.<sup>19</sup> This study emphasizes on looking for nocardia bacteraemia in a country like India with high TB prevalence along with now increasing incidence of malignancies. Species identification of *Nocardia* is essential due to different susceptibilities and resistance to the antibiotics.<sup>3,13</sup> *N. nova* complex was the commonest cause of bacteraemia in a study done by Agterof et al.<sup>14</sup> Our patient grew *N.otitidiscaviarum* in blood. This is first reported case of bacteraemia in India due to *N.otitidiscaviarum* as per best of our knowledge. Infection by *N.otitidiscaviarum* is

rare compared with other species of *Nocardia* and rarely causes infection in humans, even in immunocompromised patients.<sup>20–22</sup>

An attempt should be made to perform the antimicrobial susceptibility for each isolate too. *N. otitidiscaviarum* tends to be resistant to trimethoprim-sulfamethoxazole, but it is usually sensitive to amikacin and minocycline.<sup>23</sup> However, we could not test the susceptibility for our isolate. E test and microbroth dilutions can be performed for the isolate once standardisation is done in the laboratory.<sup>5</sup> Jiao et al has described use of Next-Generation Sequencing and its clinical use.<sup>24</sup> Relapses and multiple episodes have been known to occur in cases of nocardiosis, especially in patients with underlying immunosuppression. In a study on 132 patients of nocardiosis, 4 patients had at least 2 episodes at the same or different sites over a gap of 6–26 months with similar or different *Nocardia* isolates.<sup>8</sup>

Despite significant advancements in medical care over the past 20 years, overall mortality varied from appx. 40% to 85%. This likely reflects the significant immunosuppression and comorbid status of the population affected by nocardia bacteraemia. The rarity of nocardia bacteraemia, despite nocardiosis reiterates importance of adequate and appropriate blood cultures before initiating antimicrobial therapy with prolonged incubation in laboratory is essential.

Our patient succumb due to nocardia bacteraemia and various other comorbidity including metastatic lung adenocarcinoma even before the diagnosis could be made. This entails importance of clinical suspicion and requirement of molecular diagnosis of nocardia from the blood which remains a distant possibility today due to rarity of the disease. The overall prognosis of the disease yet remains bleak. We could not perform PCR or NGS for confirmation of identification of *N. otitidiscaviarum* which is done by MALDI-ToF. Also, the susceptibility was not performed and that is a short coming of this study. Incidence of bacteraemia due to nocardia and the associated common species in India is not known yet. Large multi-centric studies may be needed to gather data to understand clinical relevance and empiric treatment for nocardia bacteraemia in the country.

#### 4. Conclusion

In the era of emerging opportunistic infections, microbiology laboratory play a pivotal role in the diagnosis and appropriate antimicrobial treatment. Diagnosis of *N. otitidiscaviarum* did not have a positive impact on the outcome of our patient, it certainly emphasised on widening the scope of the laboratory and using diverse laboratory tools for accurate and rapid diagnosis of rare and unconventional pathogens.

#### 5. Highlights

1. *Nocardia* bacteraemia is rare, seen usually among immunosuppressed patients and are associated with

high overall mortality.

2. *Nocardia otitidiscaviarum* was the cause of bacteraemia in our patient which is a known but a rare pathogen in humans. Immunosuppression due to malignancy, chemotherapy, uncontrolled diabetes were the risk factors in our patient.
3. Identification of *Nocardia* in blood culture as single agent or as a co-infective organism should not be regarded it as a contaminant especially among immunosuppressed patients.

#### 6. Source of Funding

None.

#### 7. Conflict of Interest

None.

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