

CLINICAL GROUP

## Case Report

# Pulmonary Nocardiosis in a patient with recurrent COPD exacerbations

Kelso J, Singer J\* and Kuzniar T

American Thoracic Society, American College of Physicians, University of Chicago, NorthShore, USA

Received: 08 May, 2024

Accepted: 18 June, 2024

Published: 19 June, 2024

\*Corresponding author: Singer J, American Thoracic Society, American College of Physicians, University of Chicago, NorthShore, USA, E-mail: JSinger@northshore.org, jisaacsinger@gmail.com

ORCID: <https://orcid.org/0000-0002-5982-9695>

**Keywords:** Pulmonary nocardiosis; *Nocardia*; Cavitations; Immunosuppression; Steroids; COPD

**Copyright License:** © 2024 Kelso J, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

<https://www.organscigroup.us>

## Abstract

Pulmonary nocardiosis is a rare infection with a high mortality rate. We present a case of an elderly male with severe COPD treated with repeated courses of prednisone and highlight specific factors predisposing to a *Nocardia* infection. We review literature data and advocate for early invasive testing to direct management. We underline the role of early bronchoscopy in this select population given its safety and potential diagnostic yield.

## Introduction

Pulmonary nocardiosis is a rare, slow-growing bacterial infection with a high mortality rate. The incidence of infection in the United States is roughly 500–1000 cases per year, with males at higher risk for infection at a rate of 3:1 [1]. This infection has a predilection for a specific kind of population and has been seen in increasing frequency in patients such as the one below with recurrent COPD exacerbations requiring steroid therapy. The aim of our case presentation, as it entails below, is to describe a case of pulmonary *Nocardia*, highlight the relevant risk factors that can put a patient in a susceptible population, as well as suggest diagnostic testing that could lead to higher yield and earlier uncovering of diagnosis, so as to expedite treatment initiation and in a hope to improve mortality for this very high-risk group of people within the community.

## Case presentation

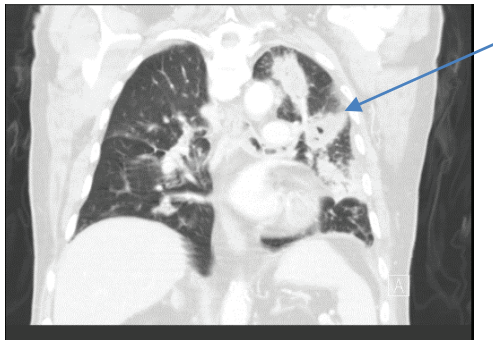
An 87-year-old male with a medical history significant for asthma/COPD with recurrent exacerbations (2–3 per year, last one 2 weeks prior to admission), hypertension, hyperlipidemia, T2DM, BPH, systolic heart failure (EF 30% – 35%), apical

aneurysm with LV thrombus on apixaban presented to the ER with shortness of breath that started 2 days prior to arrival. He had just finished a steroid taper for a COPD exacerbation secondary to respiratory syncytial virus when he noticed increasing fatigue, weakness, and a decrease in appetite. His pulmonary history was notable for multiple visits to the emergency room over the past year which indicated poor baseline control of his obstructive lung disease. He had never undergone formal pulmonary functioning testing done prior to admission, nor had prior arterial blood gas samples drawn. These were associated with productive cough and a feeling of being “unable to cough phlegm up”. He additionally endorsed some subjective fevers and a sore throat at home. The patient was originally from Mexico, immigrated in 1996, had no pets, denied recent travel, and had no sick contacts.

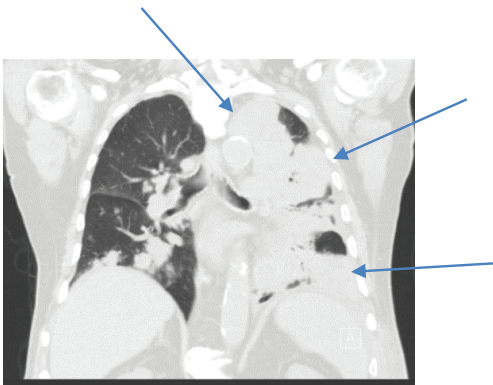
In the ER, the patient was hypotensive to 80/40 mmHg and tachycardic at 148 bpm, which both resolved with fluid boluses. The temperature was 102.3F, and it resolved with acetaminophen. The respiratory rate on admission was 34/min. He was noted to have coarse bilateral breath sounds but no increased work of breathing. Labs were notable for a significant leukocytosis 21.9 x 10<sup>3</sup>/uL with 20.5 x 10<sup>3</sup>/uL neutrophils

on differential, and serum lactic acid of 3.6 mmol/L. Chest x-ray imaging showed a left lower lobe consolidation and a small left-sided pleural effusion. A CT chest was obtained and showed multifocal confluent consolidative opacities in the left lung with cystic change, cavitation, and air-fluid levels (Image 1). These were not present on a CT scan 3 months prior to presentation. He was given prednisone 40 mg and piperacillin-tazobactam and admitted to the general medical floor.

On hospital day 1, pulmonology was consulted. Urinary *Histoplasma*, *Blastomyces*, *Legionella*, and *Streptococcus pneumoniae* antigens were sent, as well as serum procalcitonin, quantiferon, beta-3-D glucan assay, *Cryptococcus*, *Coccidioides* testing as well as sputum respiratory pathogen panel. On Hospital days 2-3 his fevers improved and his prednisone dose was reduced to 30 mg, however, he was noted to have blood-streaked sputum and oral lesions suspected to be due to a *Candida* infection. Due to minimal improvement from days 3-5, a repeat chest CT was obtained which showed worsening confluent opacifications (Image 2). A decision was made to perform a bronchoscopy with Bronchoalveolar Lavage (BAL). Quantiferon and AFB sputum both returned negative at this time. The bronchoscopy was significant for a large mucus plug in the left main stem bronchus and purulent material which was lavaged and sent for cultures. Gram stain of the lavage demonstrated branching Gram-positive rods in chains and on hospital day 9, the bronchial cultures grew *Nocardia cyriacigeorgica*.



**Image 1:** Coronal CT of the patient on presentation with note of a cavitary lesion in the left lobe.



**Image 2:** Coronal CT of the patient on hospital day 5. Note the increasing confluence of the opacities on the left, likely consistent with progressive disease.

The patient was started on imipenem-cilastatin as well as IV trimethoprim-sulfamethoxazole and underwent brain MRI, which was negative for CNS disease. He was transferred to the ICU for increased work of breathing and subsequently placed on non-invasive mechanical ventilation, which was then weaned over several days. Trimethoprim was discontinued after 3 days due to hyponatremia and hyperkalemia and switched to linezolid. After 9 days of linezolid and imipenem, pt developed severe pancytopenia and linezolid switched to amikacin out of concern for myelosuppression. In spite of these efforts, he did not improve, and with ongoing goals of care discussions with the family became abruptly bradycardic and passed away. Chest compressions were not started given the do-not-resuscitate order. The total duration from admission to death was 32 days. An autopsy was deferred per family preference.

## Discussion

Pulmonary nocardiosis is a rare Gram-positive bacillus infection that most often affects immunocompromised hosts, and thus it is often not considered when evaluating a patient with pneumonia worsening despite appropriate treatment. Our case illustrates a small but significant subset of patients with structural lung disease who are not on chronic, continuous prednisone therapy, but rather have intermittent courses of it, who develop severe and in this case fatal infection.

Previous reports [2-5] have noted a correlation between structural lung disease, recent or chronic steroid exposures, and the development of pulmonary nocardiosis. Few case reports demonstrate the rapid clinical deterioration similar to what had occurred in our otherwise stable patient over the course of several weeks. After two separate 5-day courses of glucocorticoids (576.3 mg equivalent of prednisone), in less than 4 weeks, our patient developed a fulminant *Nocardia cyriacigeorgica* infection which persisted despite cessation of steroids and multiple courses of targeted therapeutics. This could be a demonstration of a more rapidly progressive form of the disease, as opposed to a smoldering presentation. Though there is limited data on the natural history of the disease, case reports on *N. cyriacigeorgica* infection typically note significant improvement in symptoms and discharge from the inpatient setting within weeks and full recovery as noted with radiographic improvement or negative culture data in months when treated with appropriate therapy [6-13].

It is notable that this patient underwent extensive workup by pulmonary and infectious disease care teams though *Nocardia* was not considered as a potential pathogen until the patient underwent bronchoscopy. While invasive evaluation is often deferred during an initial workup of pneumonia in favor of sputum sampling, the delay in bronchoscopy in our case ultimately led to the delay in diagnosis and appropriate antimicrobial selection.

When considering the existing literature on pulmonary nocardiosis specifically *Nocardia cyriacigeorgica*, it is clear that nocardiosis is not only a disease of immunocompromised patients [2,4,14,15]. In select groups, specifically patients with structural lung disease and any glucocorticoid exposure,



it should be included in the initial differential diagnosis and investigated, as prompt treatment with appropriate agents such as trimethoprim-sulfamethoxazole can lead to more favorable outcomes [12,16–19]. Our reasoning for publishing this unique case is to advocate for a subset of patients that fit our patient's demographic and to consider early invasive testing for directed management. Structured indications for bronchoscopy sampling and testing are lacking, however, there are few contraindications to performing a bronchoscopy on a patient with a lung infiltrate that is worsening in spite of empiric therapy, and the procedure is generally well tolerated [20]. Though invasive testing is generally deferred until necessary, our patient's risk factors for an atypical disease might have prompted earlier testing.

## Conclusion

We presented this case as we found it a very prudent and useful piece of literature to be added to the growing body of evidence that highlights risk factors for pulmonary *nocardia* infections. We feel this patient fit a category of what we would consider a high-risk patient, and was managed to the utmost of current literature. Our appeal to the broader scientific community with this case report is to examine this patient's presentation and advocate for earlier invasive testing given the relative yield compared to the small assumed risk.

## References

1. Rawat D, Rajasurya V, Chakraborty RK. Nocardiosis. [Updated 2023 Jul 31]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024. <https://www.ncbi.nlm.nih.gov/books/NBK526075/>
2. Martínez Tomás R, Menéndez Villanueva R, Reyes Calzada S, Santos Durantez M, Vallés Tarazona JM, Modesto Alapont M, Gobernado Serrano M. Pulmonary nocardiosis: risk factors and outcomes. *Respirology*. 2007 May;12(3):394-400. doi: 10.1111/j.1440-1843.2007.01078.x. PMID: 17539844.
3. Baldi BG, Santana AN, Takagaki TY. Pulmonary and cutaneous nocardiosis in a patient treated with corticosteroids. *J Bras Pneumol*. 2006 Nov-Dec;32(6):592-5. English, Portuguese. doi: 10.1590/s1806-37132006000600019. PMID: 17435912.
4. Rivière F, Billhot M, Soler C, Vaylet F, Margery J. Pulmonary nocardiosis in immunocompetent patients: can COPD be the only risk factor? *Eur Respir Rev*. 2011 Sep 1;20(121):210-2. doi: 10.1183/09059180.00002211. PMID: 21881150; PMCID: PMC9584118.
5. Castellana G, Grimaldi A, Castellana M, Farina C, Castellana G. Pulmonary nocardiosis in Chronic Obstructive Pulmonary Disease: A new clinical challenge. *Respir Med Case Rep*. 2016 Mar 11;18:14-21. doi: 10.1016/j.rmcr.2016.03.004. PMID: 27144111; PMCID: PMC4840429.
6. González-Jiménez P, Méndez R, Latorre A. Pulmonary Nocardiosis. A case report. *Rev Esp Quimioter*. 2022 Apr;35 Suppl 1(Suppl 1):114-116. doi: 10.37201/req/s01.24.2022. Epub 2022 Apr 22. PMID: 35488839; PMCID: PMC9106198.
7. Qi DD, Zhuang Y, Chen Y, Guo JJ, Zhang Z, Gu Y. Interstitial pneumonia combined with nocardia cyriacigeorgica infection: A case report. *World J Clin Cases*. 2023 Nov 16;11(32):7920-7925. doi: 10.12998/wjcc.v11.i32.7920. PMID: 38073689; PMCID: PMC10698421.
8. Wu J, Wu Y, Zhu Z. Pulmonary infection caused by *Nocardia cyriacigeorgica* in a patient with allergic bronchopulmonary aspergillosis: A case report. *Medicine* (Baltimore). 2018 Oct;97(43):e13023. doi: 10.1097/MD.00000000000013023. Erratum in: *Medicine* (Baltimore). 2019 Jan;98(4):e14356. doi: 10.1097/MD.00000000000014356. PMID: 30412142; PMCID: PMC6221653.
9. Yagi K, Ishii M, Namkoong H, Asami T, Fujiwara H, Nishimura T, Saito F, Kimizuka Y, Asakura T, Suzuki S, Kamo T, Tasaka S, Gonoi T, Kamei K, Betsuyaku T, Hasegawa N. Pulmonary nocardiosis caused by *Nocardia cyriacigeorgica* in patients with *Mycobacterium avium* complex lung disease: two case reports. *BMC Infect Dis*. 2014 Dec 10;14(4):684. doi: 10.1186/s12879-014-0684-z. PMID: 25491030; PMCID: PMC4266951.
10. Manoharan H, Selvarajan S, Sridharan KS, Sekar U. Pulmonary Infections Caused by Emerging Pathogenic Species of *Nocardia*. *Case Rep Infect Dis*. 2019 Oct 1;2019:5184386. doi: 10.1155/2019/5184386. PMID: 31662925; PMCID: PMC6791275.
11. Tsuchiya Y, Nakamura M, Oguri T, Taniyama D, Sasada S. A Case of Asymptomatic Pulmonary *Nocardia cyriacigeorgica* Infection With Mild Diabetes Mellitus. *Cureus*. 2022 Apr 11;14(4):e24023. doi: 10.7759/cureus.24023. PMID: 35547411; PMCID: PMC9090208.
12. Rivera K, Maldonado J, Dones A, Betancourt M, Fernández R, Colón M. *Nocardia cyriacigeorgica* threatening an immunocompetent host; a rare case of paramediastinal abscess. *Oxf Med Case Reports*. 2017 Dec 11;2017(12):omx061. doi: 10.1093/omcr/omx061. PMID: 29255613; PMCID: PMC5726459.
13. Ninan MM, Venkatesan M, Balaji V, Rupali P, Michael JS. Pulmonary nocardiosis: Risk factors and species distribution from a high burden centre. *Indian J Med Microbiol*. 2022 Oct-Dec;40(4):582-584. doi: 10.1016/j.ijmm.2022.08.010. Epub 2022 Sep 8. PMID: 36088197.
14. Schlager R, Huard RC, Della-Latta P. *Nocardia cyriacigeorgica*, an emerging pathogen in the United States. *J Clin Microbiol*. 2008 Jan;46(1):265-73. doi: 10.1128/JCM.00937-07. Epub 2007 Nov 14. PMID: 18003809; PMCID: PMC2224293.
15. Ivashchuk G, et al. A case of *Nocardia cyriacigeorgica* lung infection presenting with a progressive obstructive ventilatory defect and worsening lung nodules in an immunocompetent host with previous history of mild bronchiectasis. In: *ATS Conference 2018 Abstracts*; 2018. Abstract B52.
16. Ott SR, Meier N, Kolditz M, Bauer TT, Rohde G, Presterl E, Schürmann D, Lepper PM, Ringshausen FC, Flick H, Leib SL, Pletz MW; OPINION Study Group. Pulmonary nocardiosis in Western Europe-Clinical evaluation of 43 patients and population-based estimates of hospitalization rates. *Int J Infect Dis*. 2019 Apr;81:140-148. doi: 10.1016/j.ijid.2018.12.010. Epub 2019 Jan 15. PMID: 30658169.
17. Takiguchi Y, Ishizaki S, Kobayashi T, Sato S, Hashimoto Y, Suruga Y, Akiba Y. Pulmonary Nocardiosis: A Clinical Analysis of 30 Cases. *Intern Med*. 2017;56(12):1485-1490. doi: 10.2169/internalmedicine.56.8163. Epub 2017 Jun 15. PMID: 28626172; PMCID: PMC5505902.
18. Mari B, Montón C, Mariscal D, Luján M, Sala M, Domingo C. Pulmonary nocardiosis: clinical experience in ten cases. *Respiration*. 2001;68(4):382-8. doi: 10.1159/000050531. PMID: 11464085.
19. Passerini M, Nayfeh T, Yetmar ZA, Coussement J, Goodlet KJ, Lebeaux D, Gori A, Mahmood M, Temesgen Z, Murad MH. Trimethoprim-sulfamethoxazole significantly reduces the risk of nocardiosis in solid organ transplant recipients: systematic review and individual patient data meta-analysis. *Clin Microbiol Infect*. 2024 Feb;30(2):170-177. doi: 10.1016/j.cmi.2023.10.008. Epub 2023 Oct 19. PMID: 37865337.
20. Bellinger CR, Khan I, Chatterjee AB, Haponik EF. Bronchoscopy Safety in Patients With Chronic Obstructive Lung Disease. *J Bronchology Interv Pulmonol*. 2017 Apr;24(2):98-103. doi: 10.1097/LBR.0000000000000333. PMID: 28005831.