

# Characteristics and Outcomes of Nocardiosis in a Solid Organ Transplant Cohort

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## ABSTRACT

**Background:** Solid organ transplant (SOT) recipients are at increased risk for nocardiosis, an infection associated with high risk of relapse and/or mortality. Novel antimicrobial regimens may be associated with improved outcomes. Here we describe a cohort of SOT recipients with *Nocardia* infection, to address knowledge gaps regarding the epidemiology of, risk factors for, and outcomes of nocardiosis in SOT.

**Methods:** This is a single center retrospective study performed at a 700-bed academic transplant center. Cases of nocardiosis were identified via review of microbiology laboratory records; transplant status was ascertained via the electronic medical record. All SOT recipients with a culture growing *Nocardia* species between 1/1/2007 and 12/31/2019 were included.

**Results:** We identified 27 SOT recipients with nocardiosis. The incidence of nocardiosis increased over the study period (Figure 1). Demographic data are shown in Table 1. Induction immunosuppression varied; 37% received an interleukin-2 receptor antagonist, 30% received anti-thymocyte globulin, and 18% received steroids alone. The majority of positive cultures were from respiratory specimens (63%) and the most common species identified were *N. nova* complex and *N. farcinica* (Table 2). The majority of patients were lymphocytopenic and received treatment for rejection. 92% of subjects received a sulfonamide agent as part of their treatment regimen and 73% received an oxazolidinone (Table 3). 73% of subjects had resolution of infection without relapse; 15% expired.

**Conclusions:** The epidemiology and risk factors for nocardiosis in this SOT cohort are consistent with established literature. Less than a third of cases occurred in subjects who had received lymphocyte-depleting induction immunosuppression; however, most subjects were lymphocytopenic at diagnosis. While nearly all subjects received a sulfonamide as part of their treatment, the majority also received an agent from the newer drug class of oxazolidinones. Overall outcomes were positive, but treatment varied, thus limiting the ability to determine if a particular combination regimen is beneficial. Multicenter randomized studies are needed to better address knowledge gaps particularly pertaining to treatment.

## INTRODUCTION

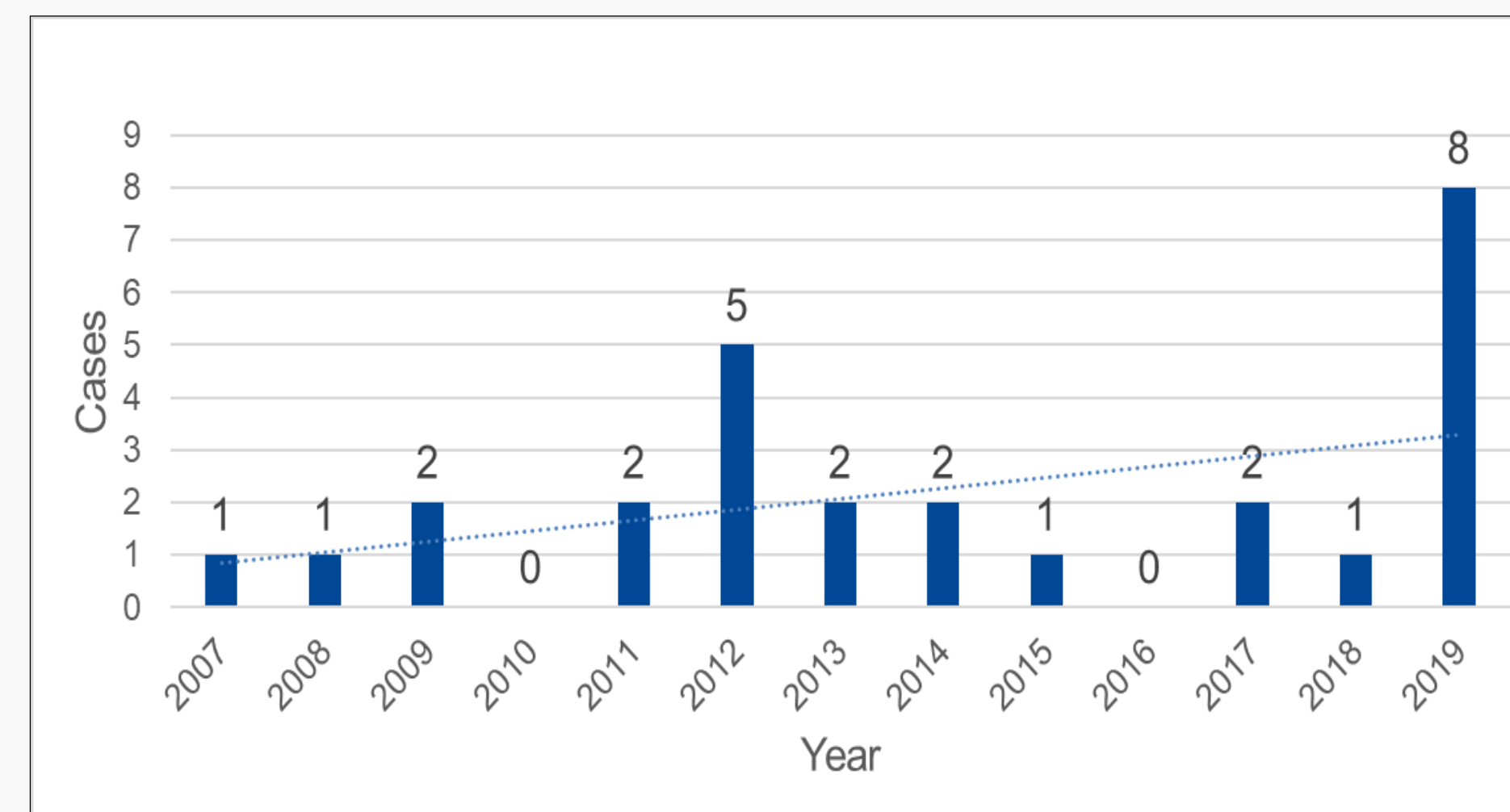
- Nocardia* infections appear to have increased in frequency in the last two decades, however epidemiologic data on nocardiosis in transplant patients is limited.
- Outcomes data for nocardiosis in SOT recipients, particularly those receiving newer antibiotic agents, is also limited.
- Our overall aim is to address knowledge gaps regarding the epidemiology of, risk factors for, and outcomes of *Nocardia* infections in SOT recipients.
- We hypothesize that there has been an overall increase in the incidence of *Nocardia* infections in the SOT population at MUSC, and that there are new, unidentified, risk factors for this infection in our patient population.

## METHODS

- This is a single-center retrospective study that was performed at the Medical University of South Carolina, a 700-bed academic medical center with comprehensive organ transplant services.
- The cohort includes all adult SOT recipients with a culture growing *Nocardia* species between 1/1/2007 and 12/31/2019.
- Transplant history and demographic data were extracted from the electronic medical record; culture data was collected from microbiology laboratory records.

- 27 patients met inclusion criteria for the study.
- There was an increased incidence of *Nocardia* infections in SOT over the 13-year study period.

**Figure 1. Epidemiologic curve**



**Table 1. Cohort demographics**

Gender, n (%)	
Male	14 (52)
Female	13 (48)
Age at transplant, years, median (range)	56 (21-76)
Organ transplanted, n (%)	
Kidney	13 (48)
Heart	4 (15)
Liver	3 (11)
Pancreas-kidney	3 (11)
Lung	2 (7)
Liver-kidney	1 (4)
Heart-kidney	1 (4)
Length of transplant hospitalization, days, median (range)	4 (2-25)*
Induction immunosuppression, n (%)	
Interleukin-2 receptor antagonist	10 (37)
Anti-thymocyte globulin	8 (30)
Methylprednisolone	5 (18)
Not available	4 (15)
Comorbid conditions, n (%)	
Diabetes mellitus	15 (56)
Structural lung disease	6 (22)

\* length of stay data not available for 4 subjects

## RESULTS

**Table 2. Infection characteristics**

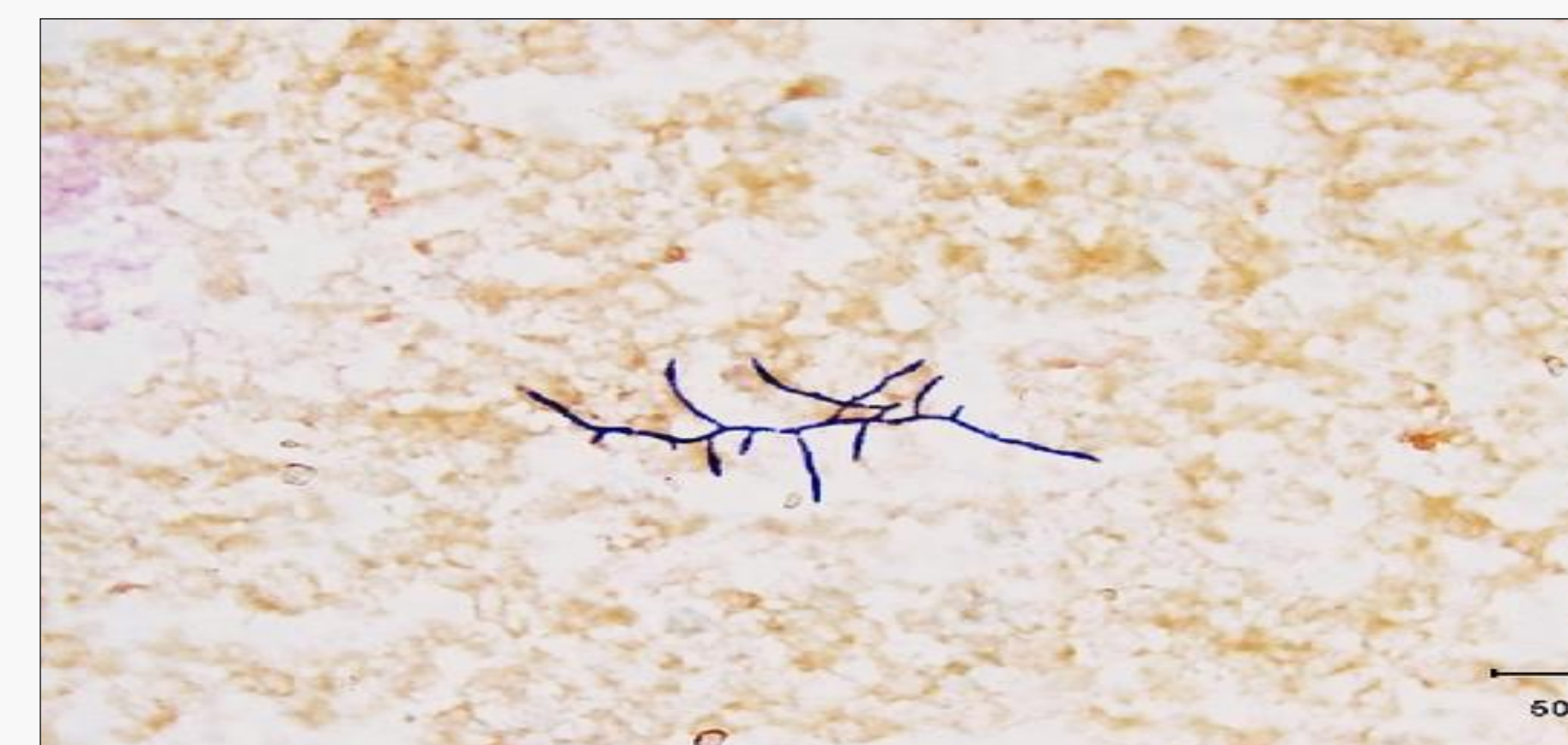
Site of positive culture, n (%)	
Lung	17 (63)
Brain	2 (7)
Skin	4 (15)
Other	4 (15)
<i>Nocardia</i> species, n (%)	
<i>N. abscessus</i> complex	1 (4)
<i>N. araoensis</i>	2 (7)
<i>N. beijingensis</i>	3 (11)
<i>N. cyriacigeorgica</i>	3 (11)
<i>N. farcinica</i>	6 (22)
<i>N. nova</i> complex	6 (22)
<i>N. pseudobrasiliensis</i>	4 (15)
<i>N. veterana</i>	1 (4)
Unable to identify to species level	1 (4)
Days from transplant to diagnosis, median (range)	397 (80-6440)
Presence of risk factors	
Absolute neutrophil count (ANC), median (range)*	6.04 (1.98-9.00)
ANC <500, n (%)*	0 (0)
Absolute lymphocyte count (ALC), median (range)*	0.63 (0.24-1.81)
ALC <1000, n (%)*	20 (80)
CMV infection prior to diagnosis, n (%)**	7 (32)
Biopsy-proven rejection prior to diagnosis, n (%)***	14 (54)
Treatment of rejection, n (%)****	
Anti-thymocyte globulin	6 (43)
Corticosteroids	11 (79)
Rituximab	1 (7)
Not documented	1 (7)

\* data not available for 2 subjects

\*\* data not available for 5 subjects

\*\*\* data not available for 1 subject

\*\*\*\* totals >100% as subjects often received more than one agent for treatment of rejection



Leli C. et al. Fatal *Nocardia farcinica* bacteremia diagnosed by matrix-assisted laser desorption-ionization time of flight mass spectrometry in a patient with myelodysplastic syndrome treated with corticosteroids. *Case Reports in Medicine*. Volume 2013. <https://doi.org/10.1155/2013/368637>

**Table 3. Treatment and outcomes**

Treatment regimens*	
Received a sulfonamide for some portion of treatment, n (%)	24 (92)
Received an oxazolidinone for some portion of treatment, n (%)	19 (73)
Maintenance immunosuppression reduced, n (%)*	22 (85)
Tacrolimus reduced/held, n (%)	5 (23)
Mycophenolate mofetil reduced/held, n (%)	10 (45)
Prednisone reduced/held, n (%)	2 (9)
More than one immunosuppressive agent reduced/held, n (%)	5 (23)
Outcome, n (%)**	
Resolution of infection without relapse	19 (73)
Relapsed infection	1 (4)
Treatment ongoing	2 (8)
Expired	4 (15)
Expired at 30 days from <i>Nocardia</i> diagnosis	1 (25)
Expired at 180 days from <i>Nocardia</i> diagnosis	3 (75)

\*treatment data not available for 1 subject

\*\*outcome data not available for 1 subject

## CONCLUSIONS

- The epidemiology and risk factors for *Nocardia* infection in this SOT cohort are consistent with established literature.
- A minority of patients had received lymphocyte-depleting induction agents; however, the majority were lymphocytopenic at the time of diagnosis.
- Sulfonamide antibiotics were the backbone treatment for most patients.
- A majority of subjects also received agents from the newer drug class of oxazolidinones, which is less well-studied for this indication.
- Overall outcomes were positive; however, the treatment regimens were too varied to assess if any agent or combination of agents was most beneficial.

## FUTURE DIRECTIONS

- Prospective data collection to build sample size, particularly given recent increased incidence.
- Case-control study to further identify risk factors.
- Multicenter retrospective study of novel therapeutic classes and drug combination treatments to identify most effective treatment regimen.