Multispecies outbreak of *Nocardia* infections in heart transplant recipients in Sydney, Australia, January 2018-August 2019: a case series

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Introduction

- *Nocardia* is an environmental aerobic actinomycete
- Infections occur via direct inoculation into the skin or via inhalation
- Diverse clinical manifestations include cutaneous, pulmonary, central nervous system and catheter-associated
- Non-cutaneous disease is most common in immunocompromised individuals, such as organ transplant recipients
- In January 2018, an increased number of *Nocardia* infections was noted among heart transplant recipients (HTR) at St Vincent's Hospital in Sydney, NSW, but not among lung transplant recipients (LTR)

Aim

To describe and compare the following aspects of *Nocardia* infections between HTR and LTR:

- Demographic characteristics
- Host risk factors
  - Underlying medical conditions
  - Immunosuppressive regimens
  - Antimicrobial prophylaxis

Methods

We identified HTR and LTR who:

1. Had a clinical culture positive for *Nocardia* species from June 2015–August 2019; and
2. Had undergone heart and/or lung transplant prior to the diagnosis of *Nocardia* infection.

Medical records were reviewed and demographic, clinical and microbiological characteristics were compared between HTR and LTR.

Results

- 18 HTR and LTR were diagnosed with *Nocardia* infections (**Figure 1**)
- Overall, the *Nocardia* isolates were susceptible to: SMX/TMP 17 (94%), linezolid 18 (100%), and imipenem 7 (54%)
  - 12 (92%) HTR isolates vs. 5 (100%) LTR isolates were susceptible to SMX/TMP
  - 8 (62%) HTR isolates vs. 2 (50%; of 4 LTR isolates with results available) were susceptible to Azithromycin

Figure 1: *Nocardia* species

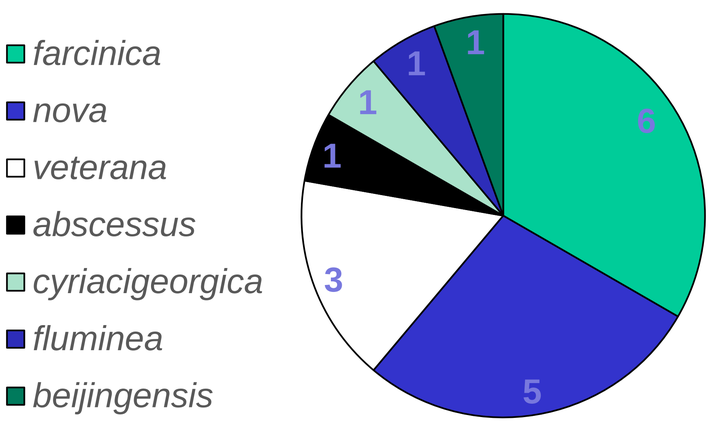

Figure 2: Nocardia cases among heart and lung transplant recipients, by date of first positive specimen

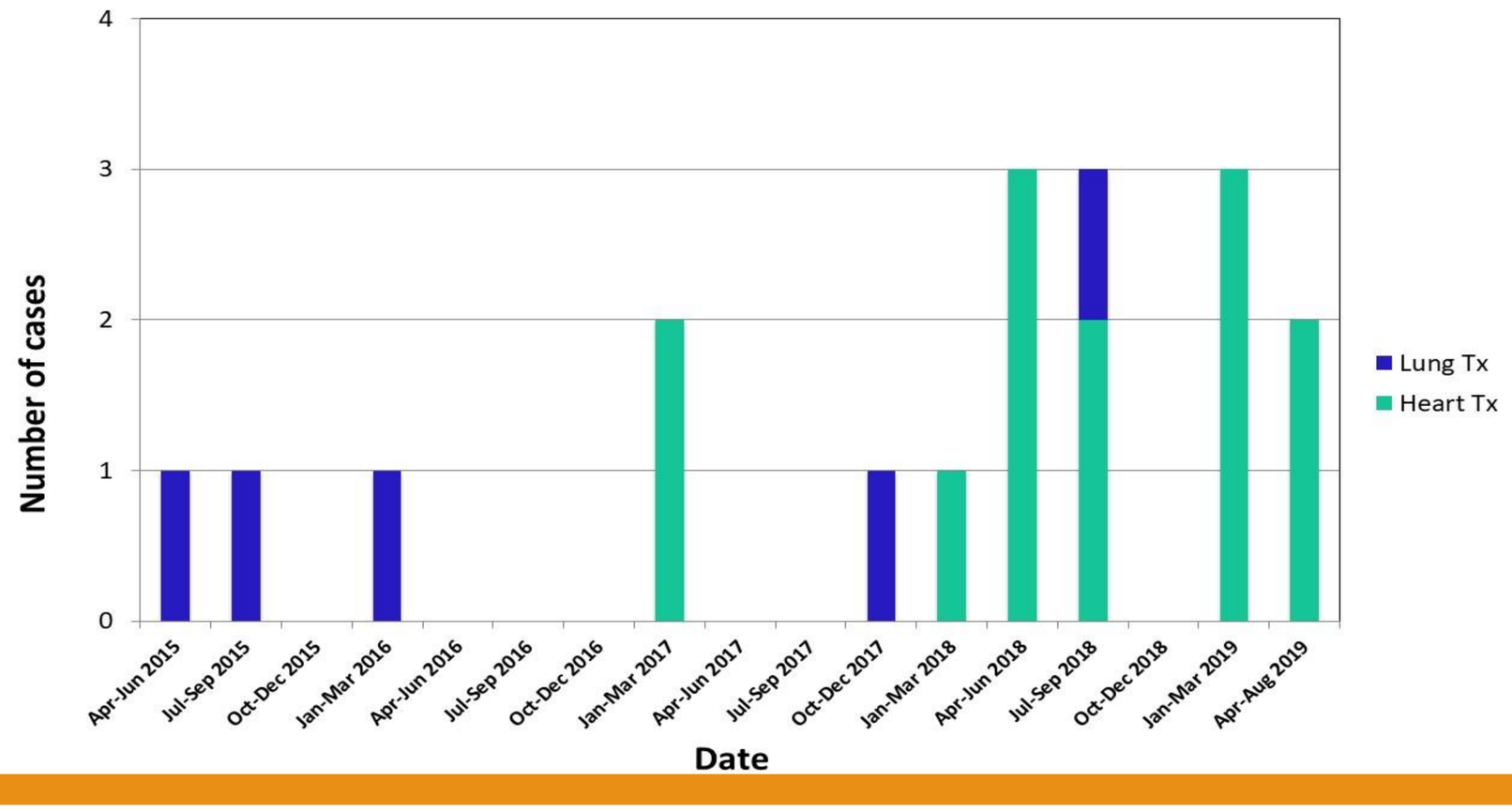

Table 1: Characteristics of *Nocardia* infections in HTR and LTR

	Heart Transplant (n = 13) n (%)	Lung Transplant (n = 5) n (%)	p-value
Induction immunosuppression with Basiliximab	13 (100)	0	<0.001
CMV mismatch at time of transplant	3 (23)	0	0.52
CMV viraemia in 6 months prior to *Nocardia* diagnosis	6 (75%) of 8 tested	0 of 4 tested	0.06
Rejection rates prior to *Nocardia* diagnosis	8 (62)	4 (80)	0.61
Sulfamethoxazole / Trimethoprim prophylaxis (800mg SMX / 160mg TMP twice weekly)	11 (85)	5 (100)	0.44
Azithromycin prophylaxis (250mg three times weekly)	0	5 (100)	<0.001

Results

- Among the 18 cases: 10 (56%) were male; Median age (range): 59 years (38-70); 17 (94%) primary pulmonary and one primary cutaneous
- **Figure 2** shows the *Nocardia* case incidence from June 2015-August 2019
  - June 2015–December 2017: 6 cases or 0.19 per month; two (33%) were HTR
  - January 2018–August 2019: 12 cases or 0.57 per month; 11 (92%) were HTR
  - During this time period, there was no change in the total numbers of heart and lung transplants performed
  - Since September 2019: 4 cases or 0.19 cases per month; 3 (75%) were HTR
- **Table 1** shows characteristics related to CMV, immunosuppression, and antibiotic prophylaxis Among HTR, 11 (85%) had diabetes; 10 (91%) of those were prednisone-induced
- Among LTR, 2 (40%) had diabetes; all were prednisone-induced
- HTR had a shorter time from transplant to *Nocardia* diagnosis than LTR (4 months vs. 23 months; p-value=0.02).

Conclusions

- *Nocardia* infections occurred earlier after transplant in HTR than LTR, more HTR had detectable CMV viremia and induction immunosuppression with basiliximab, and more LTR had azithromycin prophylaxis.
- Other unmeasured variables such as differences in exposures or environmental factors such as Australian drought conditions may also be relevant.
- Given the low rate of imipenem sensitivity, our case series suggests considering the use of empiric amikacin rather than imipenem or meropenem as recommended in the Australian Antibiotic Therapeutic Guidelines.

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