Poster # 2330

Nocardia infections in the transplanted host

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ABSTRACT (revised)

Background: *Nocardia spp* are uncommon pathogens that disproportionately afflict immunocompromised hosts. Patients who have undergone solid organ (SOT) or hematopoietic cell transplants (HCT) are at particularly high risk, but epidemiologic and outcome data for *Nocardia* infections in transplant patients are limited.
Methods: We examined a retrospective cohort of all patients between 1996-2013 (inclusive) at an academic transplant center undergoing a SOT or HCT with at least one culture that grew *Nocardia*.
Results: During the study period 52 patients were infected with *Nocardia* after transplant: 15 heart transplants (incidence 17.9/1000 transplants), 15 lung transplants (11.4/1000), 15 HCT (3.0/1000), 5 kidney transplants (2.9/1000), 1 heart-lung transplant (38.5/1000), and 1 liver transplant (1.1/1000). Subjects had a median age of 58 years (range 1-73), 73% were male, and predominantly white (71%) or African-American (25%). The median time from transplant to *Nocardia* diagnosis was 268 days (range 3-2920 days), although this varied depending on the type of transplant: 383 days for lung transplants (range 3-2507); 894 days for kidney transplants (range 108-2920), 238 days for heart transplants (range 54-1452), and 152 days for HCT (range 33-1054).
Presentation varied widely: 19% had <1 week of symptoms, 35% had symptoms for 1 week-1 month, 19% had symptoms for 1-3 months, and 8% had >3 months of symptoms (symptom duration was unknown for 19%). The lung was most often affected (85%), followed by the skin (14%) and the brain (10%); 38% of patients had infection at multiple sites. Surgical (25%) and radiographically-guided (12%) biopsies were often necessary for diagnosis. Death prior to treatment completion was common (23/52, 44%).
36.5% of the patients were taking trimethoprim-sulfamethoxazole (SMX-TMP) prophylaxis at the time of *Nocardia* diagnosis, but none of these patients had a *Nocardia* isolate with in vitro resistance to this agent.
Conclusions: *Nocardia* infection is a serious but uncommon complication in the transplanted host with a high mortality rate. It generally occurs in the late post-transplant period, but may occur while patients are still on SMX-TMP prophylaxis despite susceptibility to this agent.

METHODS

Study Aim(s): Answer the following clinical questions:

- Epidemiologic trends and timeline
- Transplant-associated risks
- Symptom duration and diagnosis
- Sites of disease
- Treatment regimens
- Susceptibility data
- Impact of SMX-TMP prophylaxis
- Outcomes

Study Design/Statistical Analysis:

- An institutional tool called DEDUCE was used to identify all patients who had undergone SOT or HCT with at least one positive culture result for *Nocardia* over an 18 year period from January 1, 1996 through December 31, 2013.
- Retrospective chart review.
- *Nocardia* was isolated from specimens sent for bacterial, fungal, and/or mycobacterial culture. Prior to 2006, isolates were generally identified locally using biochemical techniques and antimicrobial susceptibility testing was not routinely done. Since 2006, isolates were sent to the Mycobacteria/*Nocardia* Laboratory at the University of Texas, Tyler for species identification and antimicrobial susceptibility testing.
- The chi-square or Fisher's exact test were used as appropriate. The chi-square test for trend was used to assess temporal trends. Survival was evaluated using the Kaplan-Meier method, and differences in survival between groups were assessed using the log-rank test. Final outcome data were censored at death, most recent clinic appointment at Duke or December 31, 2013 (whichever was soonest).
- Statistical analysis was performed with R version 3.2.3.

RESULTS

Table 1: Patient Characteristics

Characteristic	N=52
Median age, years (Q1, Q3)	58 (43-62)
Sex, male – n (%)	38 (73)
Race - n (%)	
Caucasian	37 (71)
Black/African American	13 (25)
Other	2 (4)
HCT	15
Donor Source	
Thymus	1
Autologous	1
Matched related donor	1
Mismatched related donor	4
Matched unrelated donor	7
Umbilical cord blood	1
Conditioning Regimen	
Myeloablative	4
Non-myeloablative	10
Prior HCT	5
SOT	
Transplant Type	
Heart	15
Heart-Lung	1
Kidney	5
Liver	1
Lung (BOLT=11, SOLT=4)	15

BOLT: bilateral orthotopic lung transplant; SOLT single orthotopic lung transplant.

Tables 2 and 3: Clinical characteristics

Characteristic	N (%)
Symptom duration	
<1 week	10 (19.2)
1 week – 1 month	18 (34.6)
> 1 month but < 3 months	10 (19.2)
> 3 months	4 (7.7)
Unknown	10 (19.2)
Initial diagnostic test	
Bronchoscopy	23 (44.2)
Blood culture	1 (1.9)
Craniotomy/stereotactic brain biopsy	1 (1.9)
Open lung biopsy	6 (11.5)
Other open biopsy	6 (11.5)
Radiographically-guided needle biopsy	6 (11.5)
Skin biopsy	3 (5.8)
Sputum culture	6 (11.5)
GVHD (in HCT) and sites – at time of the *Nocardia* diagnosis	14 (93.3)
Skin	11 (78.6)
Gastrointestinal	11 (78.6)
Liver	5 (35.7)
Lung	1 (7.1)
Rejection (in SOT) – defined as in the 6 months prior to *Nocardia* diagnosis	9 (17.3%)

Characteristic	Days (range)
Time from transplant to diagnosis of *Nocardia* infection	268 (3-2920)
Heart	238 (54-1452)
Kidney	894 (108-2920)
Lung	383 (3-2507)
HCT	152 (33-1054)

Figure 1: Sites of infection

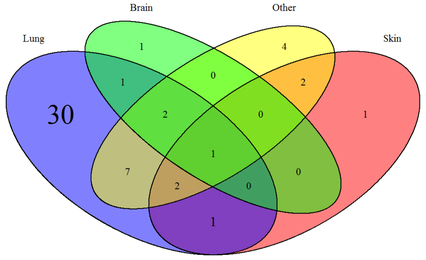
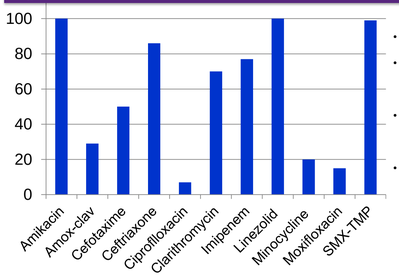


Figure 2: Susceptibilities

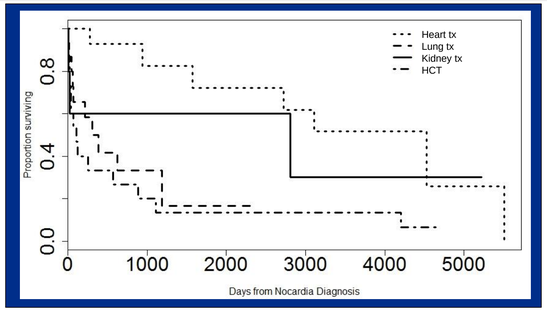


- Not all isolates were tested for susceptibilities.
- Susceptibilities were available for 43 isolates (91.5% of species) from 41 patients (78.8%).
- The most frequently isolated *Nocardia* species was *N. nova* (n=21) followed by *N. asteroides* (n=18).
- 36.5% of the patients (n=19) were taking SMX-TMP prophylaxis at infection onset.

Table 4: Treatment and outcomes

Characteristic	N (%)
Initial treatment regimen	
Treated	47 (90.4)
Monotherapy	22 (46.8)
Combination therapy	25 (53.2)
No treatment	5 (9.6)
Most frequent drugs used for initial regimen (n=47)	
SMX-TMP	40 (85.1)
Carbapenem	16 (34)
Amikacin	3 (6.4)
Other	17 (36.2)
Final outcomes	
Cured	27 (51.9)
Died	23 (44.2)
Relapse (only 47 patients with data on relapse)	2 (4.3)
Unknown	1 (1.9)

Figure 3: Survival



Kaplan-Meier curve – long term survival by transplanted organ in the SOT group

CONCLUSIONS

- *Nocardia* infection is typically a late post-transplant complication.
- Heart transplant recipients seem to have the highest incidence of *Nocardia* infections; HCT the lowest.
- Symptom duration and sites of infection vary widely.
- GVHD is often present in HCT recipients with *Nocardia* infection.
- Invasive diagnostic methods are often needed and pursued.
- The most frequently isolated species was *N. nova.*
- Infections occurred despite receipt of SMX-TMP prophylaxis but did not appear to result in SMX-TMP resistant *Nocardia* isolates.
- Overall outcomes remain poor though likely contributed to by severity of the underlying disease in this population.

REFERENCES

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