Risk Factors for *Nocardia* Infection in Heart Transplant Patients

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ABSTRACT

Infections related to *Nocardia* species occur more commonly in immunosuppressed patients, including solid organ transplant recipients. At our institution, we observed an increased incidence of *Nocardia* infection in heart transplant recipients from 2011-2013.

We performed a matched case-control study of heart transplant patients who received care at Vanderbilt University Medical Center between 2003 and 2013. Control patients were matched for duration of post-transplant follow up that corresponded to the time of the case patient's diagnosis of *Nocardia* infection. To identify risk factors associated with *Nocardia* infection, conditional logistic regression was performed to determine odds ratios (OR).

Among 331 heart transplant recipients, 11 (3%) developed infection from *Nocardia spp.* The incidence was 2.5 cases per 100 transplants from 2003-2010, but increased to 4.5 cases per 100 transplants from 2011-2013. In comparison to 60 controls, cases were more likely to have elevated blood levels of calcineurin inhibitors (OR 6.7; 95% confidence interval [CI] 1.2-36.2) and more likely to have coinciding fungal infection (OR 24.9; CI 2.9-214), cytomegalovirus (CMV) infection (OR 9.9; CI 1.01-98) and CMV disease (OR 13.9 ; CI 1.4-133). Control patients were more likely to have an absolute lymphocyte count above 1000 cells/mcL (OR 0.09; CI 0.01-0.8) and to take more tablets of sulfamethoxazole/trimethoprim as prophylaxis per week (OR 0.5 per tablet per week; CI 0.26-0.97). Heart recipients who were transplanted from 2011-2013 were significantly more likely to have received antithymocyte globulin induction, higher dosages of mycophenolate mofetil, higher dosages of corticosteroids, and to have lower lymphocyte counts compared to those transplanted prior to 2011.

We observed an increased incidence of *Nocardia* infections in heart transplant recipients beginning in 2011. Compared with controls, infected patients had elevated levels of calcineurin inhibitors, significantly lower absolute lymphocyte counts, and coinciding infections with fungus and CMV. The data suggest that intensified immunosuppression for heart transplant recipients resulted in a significant increase in *Nocardia* infections.

BACKGROUND

- *Nocardia spp*: gram positive filamentous bacteria
- Infections occur more commonly in immunosuppressed patients
- Solid organ transplant well documented risk factor (incidence 0.04 – 3.5 %)
- Increased incidence observed at Vanderbilt University Medical Center from 2011-13 in heart transplant recipients

METHODS

- All cases of *Nocardia spp* infections in heart transplant recipients at Vanderbilt University Medical Center identified from 2003-2013
- Retrospective, matched case-control study: controls matched for duration of post transplant follow up corresponding to time of case patient's infection
- Conditional logistic regression performed to identify risk factors associated with *Nocardia* infection

RESULTS

- Among 331 heart recipients, 11 (3%) developed Nocardia infection
- 2003-2010 incidence: 2.5 per 100 transplants
- 2011-2013 incidence: 4.5 per 100 transplants

Table 1. Risk factors for developing *Nocardia* infection

Characteristic	Odds Ratio of Association with Infection	95% Confidence Interval
Age	1.06	0.98-1.13
AA Race	3.47	0.88-13.68
High CI Level	6.71	1.24-36.2
Steroid Dosage (per mg Prednisone)	1.07	0.95-1.20
Rejection Treatment	0.66	0.15-2.92
Bactrim (per DS tab per week)	**.51**	**0.26-0.97**
Coinciding Infection	**16.4**	**3.4-78.3**
Invasive Fungal Infection	**24.9**	**2.9-213.9**
CMV Infection	**9.94**	**1.01-98.1**
CMV Disease	**13.9**	**1.44-133.3**
ALC > 1000	**0.09**	**0.011-0.08**
Valganciclovir Prophylaxis	4.53	0.92-22.4

Table 2. Differences in patient characteristics pre and post 2011

Characteristic	2003-10 (n=33)	2011-13 (n=38)	p
Tacrolimus	**55%**	**97%**	**<.001**
ATG induction	**37%**	**88%**	**<.001**
MMF	84%	79%	.76
Median MMF dose	**2160mg**	**3000mg**	**0.2**
Glucocorticoids	**61%**	**85%**	**.03**
Median steroid dose	**5 mg**	**12.5 mg**	**.002**
Rejection treatment	**24%**	**48%**	**.046**
Valcyte	**11%**	**42%**	**.003**
Mean WBC	5670	6125	0.3
Mean ANC	4030	4630	0.27
Mean ALC	**910**	**530**	**.0008**
On Bactrim DS TIW	**13%**	**54%**	**<.001**

CONCLUSION

- Increased incidence of *Nocardia* infections in heart transplant recipients beginning in 2011 at our medical center
- Infected patients had more elevated levels of calcineurin inhibitors, lower absolute lymphocyte counts, and coinciding infections with fungus and CMV
- Intensified immunosuppression of heart transplant recipients likely resulted in increase of *Nocardia* infections