A Case of a Kidney Transplant Recipient with Pulmonary Cytomegalovirus and Nocardia Coinfection with Cytomegalovirus Nephropathy

Inwhee Park, M.D.¹, Hyunee Yim, M.D.², Lim Seung-Kwan, M.D.³, Sukyong Yu, M.D.¹, Jinhee Cho, M.D.¹, Heungsoo Kim, M.D.¹ and Gyu-Tae Shin, M.D.¹

Departments of Nephrology¹, Pathology², Pulmonary and critical Care Medicine³
Ajou University School of Medicine, Suwon, Korea

This is the first reported case of a kidney transplant patient in Korea who developed cytomegalovirus and Nocardia pulmonary coinfection simultaneously with cytomegalovirus nephropathy. The patient had a history of end stage renal disease on peritoneal dialysis, diabetes mellitus and pulmonary tuberculosis. He underwent unrelated living kidney transplantation in China. About 5 months after transplantation, he developed high fever and rising serum creatinine for which he was admitted to hospital. Chest CT revealed consolidation in the left upper lung field and lung biopsy showed CMV infected bronchiolitis obliterans with organizing pneumonia. Culture of lung biopsy tissue grew Nocardia farcinica. In addition, he was found to have CMV infection in kidney tissue with positive CMV antigen assay of blood. This case emphasizes that CMV infection, through its effect on systemic immunity, may increase the risk of opportunistic infection.

Key Words: Cytomegalovirus, Nocardia, Kidney transplantation

INTRODUCTION

Cytomegalovirus (CMV) has a variety of direct effects, including tissue injury and clinical disease, and indirect pathogenic effects in transplant recipients. One of indirect effects of CMV infection is CMV-mediated immune deficits, the patient is rendered more susceptible to opportunistic infection. Thus, in a patient with unusual infection, the possibility of CMV as a cofactor must be considered. Herein, we report a case of pulmonary infection with CMV and Nocardia farcinica simultaneously developed with CMV nephropathy in a renal transplant recipient.

CASE REPORT

A 53-year-old gentleman who had a history of end stage renal disease on peritoneal dialysis, diabetes mellitus and high blood pressure, underwent living unrelated kidney transplantation in China. He suffered from pulmonary tuberculosis while on peritoneal dialysis which was successfully treated with an antituberculosis regimen. He was CMV-IgM negative and CMV-IgG positive, but the CMV serostatus of the kidney donor was unknown. His immunosuppressive medications included tacrolimus (FK 506), mycophenolate mofetil, and prednisolone. On the 9th day after the operation, he came back to our clinic for follow up and was added on 80

Submitted: 29 October 2008, Accepted: 13 January 2009
Correspondence: Gyu-Tae Shin, M.D.
Ajou University School of Medicine, Department of Nephrology, Youngtong-gu, Wonchon-dong, San 5, Suwon, 442-749, South Korea
Tel: 031/219-5131, Fax: 031/219-5137
E-mail: gtshin@ajou.ac.kr
mg/400 mg trimethoprim–sulfamethoxazole a day for infection prophylaxis while maintaining the same immunosuppression regimens. About 24 days after kidney transplantation, he was found to have CMV viremia by polymerase chain reaction (PCR). However, he denied all symptoms of CMV disease. His serum creatinine level was around 1.4–1.5 mg/dL and FK 506 level was 10 ng/mL. His creatinine clearance by Cockcroft–Gault equation was 46.7 mL/min. Prednisolone dose was reduced and he was given valganciclovir (Valcyte) 900 mg a day for approximately two and a half months, which eradicated CMV viremia successfully. On the 161st day after transplantation, the patient was admitted because of high fever for five days. But he denied headache, blurred vision, chest pain, cough and diarrhea. Chest radiographs showed an opaque lesion in the left upper lung field. His serum creatinine level, which had been around 1.4–1.7 mg/dL, rose to 2.1 mg/dL. Chest computed tomography revealed irregular consolidation in the left upper lung field without ground-glass opacity and subsequent needle aspiration lung biopsy revealed CMV infected bronchiolitis obliterans with organizing pneumonia. Additionally, culture of tissue obtained from lung biopsy grew Nocardi a farcinica (Fig. 1, 2, 3A). Biopsy of the transplanted kidney revealed CMV infection, no evidence of rejection and acute tubular necrosis (Fig. 3B). CMV antigen assay of blood was found to be positive again. Subsequently, FK506 dose was reduced, MMF was discontinued and intravenous ganciclovir 250 mg a day and intravenous trimethoprim–sulfamethoxazole (TMP–SMX) 320 mg/1600 mg a day were started. After 5 days, Se-

Fig. 1. Chest CT shows irregular consolidation in the left upper lung.

Fig. 2. Modified AFB stain of Nocardi a farcinica in aspirated lung tissue, which shows acidfast stain of long-branching forms.

Fig. 3. Pathologic diagnosis of cytomegalovirus infection. (A) Histochemical staining specific for the cytomegaloviral antigen in aspirated lung tissue (arrow) (magnification, × 400). (B) A large cytomegalovirus infected cell in a glomerulus (arrow) (H&E; magnification, × 400).
rum white blood cell counts were reduced from 6,000/
µL to 2,600/µL. Intravenous ganciclovir was reduced to
200 mg a day and white blood cell counts were nor-
malized. While on this treatment, CMV antigenemia
became negative and the serum creatinine level which
had risen to 2.5 mg/dL was stabilized at 1.9–2.1 mg/
dL. The patient remained afebrile and the pulmonary
findings improved. He was discharged home on the 22nd
day of admission.

**DISCUSSION**

The most important pathogen affecting transplant
recipients is CMV, which causes both direct effects
and a variety of indirect effects. The direct effects
include various organ invasion including pneumonia,
nephritis, neutropenia, thrombocytopenia, colitis, gas-
tritis, ulcers with bleeding or perforation, pancreatitis
and chorioretinitis. But one of the controversial issues
regarding CMV infection in renal transplantation is
whether the virus itself can cause allograft renal dys-
function. When allograft renal function deteriorates
in patients with CMV infection, factors such as de-
creased allograft renal perfusion, acute tubular necrosis,
and transplant rejection may be more important than
a direct viral effect on the transplanted kidney. The
indirect effects of CMV infection are produced by a
profound suppression of host defenses which predis-
poses to secondary invasion by other pathogens such as
*Pneumocystis, Candida*, bacteria, *Aspergillus* spe-
cies, and *Nocardia* species.

CMV also contributes to the risk of graft rejection,
post transplant leukoproliferative diseases, human her-
pesvirus (HHV6) and HIV7 infections, and acceler-
a
tion of hepatitis C virus infection. The mechanisms
for these effects are complex, including alteration of
T-cell numbers and functions, and of major histo-
compatibility complex (MHC) synthesis as well as the
induction of an array of proinflammatory cytokines,
chemokines, and growth factors. Given these facts, it
is conceivable that CMV infection might produce an
immune milieu which increases susceptibility to No-
cardia infection and ultimately led to simultaneous in-
fec tion of such an unusual organism in this case.

*Nocardia* species are ubiquitous environmental sar-
rophytes living in soil, organic matter and water. Inhalation of the organism appears to be the main
route of transmission but penetrating cutaneous injury
is another route of inoculation. In these patients,
immunosuppression is the major risk factor for No-
cardia infection and for the same reason, patients with
CMV infection, HIV–infection, lymphoreticular malig-
nancies, or those treated with chronic corticosteroid
therapy are also susceptible for this infection. Although
*Nocardia* infection usually occurs during one
to six months after organ transplantation as seen in
our patient, the diagnosis should be considered anytime
if aggressive immunosuppression such as lymphocyte
antibodies has been previously used. The definitive
diagnosis of *Nocardia* disease requires demonstration
of the organism on culture from a suspected site. *No-
cardia* is a Gram–positive, aerobic, branching bacteria
usually stain with a modified acid–fast stain and they appear in tissue sections as Gram–posi-
tive branching and beading rods. The classification
of *Nocardia* infection is based upon the location and
extent of disease and includes pulmonary, central nerv-
ous system, cutaneous, and disseminated disease. Al-
though there are no pathognomonic signs or symp-
toms of *Nocardia* infection, it should be suspected in
any patient who presents with brain, soft tissue, or
cutaneous lesions, and a concurrent or recent pulmo-

- 163 -

nary process. The lungs are the primary site of *Nocar-
dia* infection in more than two-thirds of cases. *No-
cardia* are not normally found in the respiratory tract.
As a result, isolation of *Nocardia* from the sputum is
almost always indicative of infection. Most pulmonary
infections are primary but *Nocardia* can spread to the
lung from other sites, such as the skin. The onset
of pulmonary nocardiosis may be acute, subacute,
chronic and is not distinguished by any specific signs
or symptoms. Fever, night sweats, fatigue, anorexia,
weight loss, dyspnea, cough, hemoptysis, and pleuritic chest pain have all been described. A multitude of radiographic findings have been demonstrated in pulmonary nocardiosis, including single or multiple nodules, lung masses (with or without cavitation), reticulonodular infiltrates, interstitial infiltrates, lobar consolidation, subpleural plaques, and pleural effusions. As a result, pulmonary nocardiosis has frequently been misdiagnosed initially as tuberculosis (since upper lobe involvement is common and Nocardia species are weakly acid-fast), invasive fungal disease, and malignancy. TMP–SMX is the preferred agent in treating Nocardia infections. Alternative regimens are imipenem, amikacin, ceftiraxone, minocycline, ciprofloxacin and amoxicillin/clavulanate. Initial selection of antibiotic therapy should take into account the site and severity of disease, the potential drug interactions and the species of Nocardia.

Given the rapidly increasing population of immunocompromised patients, Nocardia infection is likely to continue to be an important opportunistic disease. To our knowledge, this is the first reported case of a kidney transplant patient who developed CMV and Nocardia pulmonary infection simultaneously with CMV nephropathy in Korea. This case emphasizes that CMV infection, through its effect on systemic immunity, can be an important cofactor in the development of Nocardia infection.

REFERENCES
