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# Clinical Outcomes of *Pneumocystis carinii* Pneumonia in Adult Liver Transplant Recipients

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ABSTRACT

Purpose. *Pneumocystis carinii* pneumonia (PCP) is an opportunistic infection associated with morbidity and mortality in solid-organ transplant recipients. We retrospectively assessed the characteristics and outcomes of liver transplant (OLT) recipients with PCP compared with those of patients with severe non-*P carinii* pneumonia (non-PCP) who required intensive care with mechanical ventilation.

Methods. During the 2-year period between January 2008 and December 2009, 43 adult OLT recipients had severe pneumonia requiring mechanical ventilation; of these, 8 (19%) had PCP. During this period, routine antibiotic prophylaxis was administered for the first 6 months after OLT.

Results. The median period from OLT to development of PCP was 9.5 months (range, 1–67); the 1-year incidence was 0.9%. The 6 and 6 to 12-month incidences of non-PCP were 4.2% and 0.3%, respectively, and those of PCP were 0.3% and 0.6%, respectively. Four of 8 patients (50%) in the PCP group had a recent history of a rejection episode. PCP was associated with a higher incidence of prior antirejection treatment. There were no significant differences between PCP and non-PCP groups in age, gender, preoperative Model for End-stage Liver Disease score, primary diagnosis, graft type, and total number of rejection episodes.

Conclusions. These results indicate that the risk of PCP in OLT recipients is closely related to strong immunosuppressive treatment for acute cellular rejection episodes, suggesting the importance of PCP prophylaxis in these patients. Because most patients developed PCP at around 1 year, it may be advisable to prolong routine post-OLT PCP prophylaxis for 12 months, especially among patients receiving antirejection treatment.

PNEUMOCYSTIS CARINII (PC) is an opportunistic pathogen that can cause a severe form of pneumonitis in solids-organ transplant recipients and other immunocompromised hosts. The incidence of PC infection may be as high as 10% during the first 6 months after transplantation.[1] The risk is greatest during this early post-transplant period and also during periods of increased immunosuppression.[2] Although a vaccine is not yet available, treatment with trimethoprim (TMP)-sulfamethoxazole (SMX) has been shown to be a safe and effective specific prophylaxis against PC infection in patients infected with human immunodeficiency virus (HIV), in cancer patients, and in transplant recipients.[3–5]

In the absence of prophylactic treatment, the incidence of PC pneumonia (PCP) in liver transplant (OLT) recipients has been estimated at 3% to 11%. If left untreated, mortality from PCP approaches 100%. Despite appropriate therapy, the mortality rate can still reach up to 30%. Therefore, PC prophylaxis is essential in patients at high risk of opportunistic infection.[6]

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**Table 1. Clinical Features of Liver Transplant Recipients With Severe Pneumonia**

| | PCP group ($n = 8$) | Non-PCP group ($n = 35$) | *P* value |
|---|---|---|---|
| Age (ys) | 52.4 ± 7.8 | 51.6 ± 10.4 | .81 |
| Gender | | | |
| Male | 4 | 25 | |
| Female | 4 | 10 | |
| MELD | 22.0 ± 10.1 | 29.1 ± 8.8 | .09 |
| Child-Turcotte-Pugh | 10.8 ± 3.3 | 11.4 ± 2.3 | .58 |
| Time to onset of pneumonia (mo) | | | .37 |
| Mean ± SD | 7.8 ± 21.3 | 15.4 ± 18.3 | |
| Median (range) | 9.5 (1–67) | 2.0 (1–106) | |
| Type of liver transplantation | | | .23 |
| Living donor | 7 | 23 | |
| Right lobe | 6 | 19 | |
| Left lobe | | 1 | |
| Dual lobe | 1 | 2 | |
| Deceased donor | 1 | 12 | |

PCP, *Pneumocystis carinii* pneumonia; MELD, Model for End-stage Liver Disease; SD, Standard deviation.

Although OLT recipients at our center received routine PC prophylaxis, not a few patients have experienced serious manifestations of PCP. We assessed the clinical characteristics of OLT recipients with PCP and compared their outcomes with those of patients with non-PCP, all of whom required intensive care with mechanical ventilation.

## MATERIALS AND METHODS

The study was a retrospective study on patients with PCP at a high-volume OLT center that performs more than 300 OLTs per year.[7] According to our institutional protocol on OLT management, all adult OLT recipients received primary PC prophylaxis with TMP-SMX, consisting of double-strength tablets (160 mg TMP/800 mg SMX) once every other day during the first 6 months after OLT.

During the 2-year study period between January 2008 and December 2009, 670 adult OLTs were performed, and more than 2000 adult OLT recipients were followed at the outpatient clinic. During this time, 43 adult OLT recipients ≥18 years of age were diagnosed with severe pneumonia requiring mechanical ventilatory care. PCP diagnosis was confirmed by positive methenamine silver staining or by specific monoclonal antibody immunofluorescence tests using bronchoalveolar lavage samples or sputum specimens.

Data on acute rejection episodes were collected. Acute cellular rejection was confirmed using the Banff rejection activity index.[8] Transjugular liver biopsies were preferentially performed.[9] This study protocol was approved by the Institutional Review Board of the Asan Medical Center. Incidences were compared using the chi-square test and Fisher exact test, and *P*-values less than .05 were considered statistically significant.

## RESULTS

### Patient Profiles

During the study period, a total of 43 OLT adult recipients with severe pneumonia were consecutively admitted to the surgical intensive care unit. The overall incidence of severe pneumonia requiring mechanical ventilation was 4.5% (30/670) before post-transplant 6 months and 0.9% (6/670) between 6 and 12 months, resulting in 1-year incidence of 5.4%. Severe pneumonia occurred in only 7/>2000 patients followed for more than 1 year (<0.4%). Of them, 8 (19%) were diagnosed with PCP, making its incidences 0.3 (2/670) within post-transplant 6 months, 0.6% (4/670) between 6 and 12 months, and <0.1% (2/>2000) after 1 year. The incidences of non-PCP were 4.2% (28/670) within post-transplant 6 months, 0.3% (2/670) between 6 and 12 months, and <0.3% (5/>2000) after 1 year.

The clinical characteristics of these patients (PCP group) were compared with those of the 35 non-PCP patients (non-PCP group). All patients received TMP-SMX for PCP prophylaxis. The clinical profiles of these two groups are summarized in Table 1.

In the 8 patients with PCP, the median time from OLT surgery to the onset of PCP was 9.5 months (range: 1–67 months) and the mean time (±standard deviation) was 7.8 ± 21.3 months. Six patients developed PCP during the first year after OLT. Two developed PCP within the first 6 months after OLT while receiving TMP-SMX prophylaxis, whereas the other 4 developed PCP 6 to 12 months after OLT. The other 2 patients were diagnosed with PCP 13 and 67 months, respectively, after OLT (Table 2).

### Association With Rejection Episodes

Four of 8 patients with recent rejection episodes received more intensive immunosuppressive treatment (Table 2). Despite severe pneumonia, patients 1 and 4 received intensive immunosuppressive treatment because of acute cellular rejection from liver biopsy. Their peak trough levels of immunosuppressants were tacrolimus 17.0 ng/mI and cyclosporine 190 ng/mL. Patient 3 received tacrolimus 5 mg twice

**Table 2. Profile of Patients With *Pneumocystis carinii* Pneumonia (PCP)**

| Case | Gender | Age (ys) | Time to diagnosis PCP (mo) | Type of liver transplantation | Recent episode of rejection | Outcome |
|---|---|---|---|---|---|---|
| 1 | M | 43 | 1 | Living donor | Present | Dead due to PCP |
| 2 | F | 51 | 2 | Living donor | Absent | Alive after cure |
| 3 | M | 52 | 9 | Living donor | Present | Dead due to PCP |
| 4 | M | 55 | 9 | Living donor | Present | Dead due to PCP |
| 5 | M | 54 | 10 | Living donor | Absent | Alive after cure |
| 6 | F | 55 | 12 | Living donor | Absent | Dead due to PCP |
| 7 | F | 42 | 13 | Living donor | Absent | Alive after cure |
| 8 | F | 67 | 67 | Deceased donor | Present | Alive after cure |