MAJOR ARTICLE

Risk Factors, Clinical Features, and Outcomes of Listeriosis in Solid-Organ Transplant Recipients: A Matched Case-Control Study

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Background. Solid-organ transplant (SOT) recipients are classically considered to be at increased risk for listeriosis. However, risk factors for this infection have not been assessed.

Methods. We carried out a multicenter, matched case-control study (1:2 ratio) from January 1995 through December 2007. Control subjects were matched for center, transplant type, and timing. Conditional logistic regression was performed to identify independent risk factors. Clinical features and outcomes for all case patients were reviewed.

Results. Thirty patients (0.12%) with cases of listeriosis were identified among 25,997 SOT recipients at 15 Spanish transplant centers. In a comparison of case patients with 60 matched control subjects, the following independent risk factors for listeriosis were identified: diabetes mellitus (odds ratio [OR], 5.6; 95% confidence interval [CI], 1.6–19.6; $P = .007$), history of cytomegalovirus infection or disease within the preceding 6 months (OR, 35.9; 95% CI, 2.1–620; $P = .014$), receipt of high-dose prednisone within the preceding 6 months (OR, 6.2; 95% CI, 1.8–21.1; $P = .003$), and trimethoprim-sulfamethoxazole (TMP-SMZ) prophylaxis (OR, 0.07; 95% CI, 0.006–0.76; $P = .029$). Twenty-six patients (86.7%) had bacteremia, and 7 had shock at presentation. Other manifestations included meningoencephalitis (10 cases), spontaneous peritonitis (2), pleural empyema (1), brain abscesses (1), and liver abscesses (1). The 30-day mortality rate was 26.7% (8 of 30 patients died).

Conclusions. Listeriosis in SOT recipients is uncommon but causes high mortality. Diabetes mellitus, cytomegalovirus infection or disease, and receipt of high-dose steroids are independent risk factors for this infection, whereas TMP-SMZ prophylaxis is a protective factor.

Listeria monocytogenes is an environmental gram-positive, motile bacillus which has the ability to survive and multiply in phagocytic host cells. The main route of infection acquisition is through the intestinal tract after ingestion of contaminated food products, as well as from mother to child, either transplacentally or during childbirth. *L. monocytogenes* is a rare cause of illness among the general population. However, for some groups, including newborn infants, pregnant women, elderly patients, and immunocompromised hosts, in particular, this organism is an important cause of life-threatening bacteremia and meningoencephalitis [1].

Solid-organ transplant (SOT) recipients are typically considered to be at increased risk for acquiring listeriosis because of immunosuppressive therapy–related deficiencies in cellular immune function [2, 3]. Nevertheless, although cases of listeriosis occurring in SOT recipients have been sporadically reported [4–9], comprehensive information on this infection in this pop-

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ulation is particularly scarce. Significantly, risk factors for listeriosis in SOT recipients have not been formally assessed. We conducted the present multicenter study to identify the risk factors for sporadic listeriosis in SOT recipients with a 1:2 matched case-control study design and to review the clinical features, microbiological characteristics, and outcomes for all case patients.

MATERIALS AND METHODS

Setting and study population. The study was conducted in 15 Spanish tertiary care hospitals with active organ transplantation programs, including liver, kidney, heart, lung, pancreas, intestinal, and multivisceral transplantation. All patients with culture-proven listeriosis from January 1995 through December 2007 were included in the analysis. Patients were identified from the hospital microbiology and transplantation program databases; initial identification was followed by a detailed review of patient medical records. The study was approved by the institutional review boards of the participating transplantation centers.

For the purposes of risk factor analysis, a matched case-control study (1:2 ratio) was performed. Two control subjects were included for each case patient with listeriosis. The control subjects were matched for 3 characteristics: (1) institution, (2) type of transplantation, and (3) time of transplantation. The recipients who underwent transplants immediately before and after the index case patient and who survived at least as long as the time to diagnosis of listeriosis were categorized as control subjects.

Clinical data and definitions. For the case patients, the "time of event" was defined as the time of *Listeria* infection diagnosis; for the control subjects, the time of *Listeria* infection in the corresponding case patient was used. Variables analyzed for both case patients and control subjects included patient demographic data, transplant type, prior transplantation, presence of diabetes mellitus, immunosuppressive drugs at the time of the event, an elevated mean calcineurin inhibitor level within the preceding 30 days (>15 μg/mL for tacrolimus and >300 ng/mL for cyclosporin), history of high-dose prednisone therapy within the preceding 6 months ($\geq$20 mg of prednisone for $\geq$1 month or >2 pulses of 1 g of intravenous methylprednisolone), receipt of a lymphocyte-depleting antibody within the preceding 12 months, trimethoprim-sulfamethoxazole (TMP-SMX) prophylaxis at the time of the event, allograft rejection within the preceding 6 months, history of cytomegalovirus (CMV) infection or disease within the preceding 6 months, mean lymphocyte and neutrophil counts within 30 days of the event, and mortality rates at 30 days and 1 year after the event.

For all case patients, clinical characteristics and laboratory data at the time of *Listeria* infection, treatment, and outcomes were exhaustively evaluated. Hypoalbuminemia at the time of *Listeria* infection was considered to be present when the serum albumin level was <3 g/L. Renal impairment was defined as a serum creatinine level >1.5 mg/dL. Meningoencephalitis was considered to be present in case of culture-proven *Listeria* infection and suggestive neurological symptoms not attributable to any other etiology, even if cerebrospinal fluid (CSF) cultures had negative results or were not performed. CMV infection was diagnosed by growing the virus in vitro, finding evidence of viral infection by intracytoplasmic or intranuclear inclusions or by antibody-based staining techniques for CMV in histopathologic sections or by finding evidence of replication using nucleic acid–based assays or antigenemia studies. CMV disease was defined as evidence of CMV infection with attributable symptoms, as described elsewhere [10].

Microbiological studies. Each hospital's microbiology laboratory identified organisms as *L. monocytogenes* and performed susceptibility testing. *L. monocytogenes* strains were identified according to their colony characteristics, Gram stain morphology, motility, catalase activity and conventional microbiological procedures [11]. Serotyping was performed using specific antisera (Difco; Becton Dickinson). Susceptibility testing was performed with the microdilution method according to the guidelines of the Clinical Laboratory Standards Institute 2006 [12]. The strains with minimal inhibitory concentration (MIC) of ampicillin $\leq$2 mg/L and MIC of TMP-SMZ ($\leq$0.5 and $\leq$9.5 mg/L), were considered to be susceptible according to Clinical Laboratory Standards Institute criteria.

Statistical analysis. To detect statistically significant differences between specified groups, we used the χ^2 test with continuity correction for categorical variables and the Student's *t* test for continuous variables. Univariate odds ratios (OR) were calculated for the potential risk factors for *Listeria* infection. Multivariable conditional logistic-regression analysis of factors potentially associated with *Listeria* infection included all statistically significant variables in univariate analysis and all clinically important variables, whether they were statistically significant or not [13]. The analysis was performed with the stepwise logistic-regression model of the SPSS software package (SPSS). The Mantel-Haenszel test was used to analyze trends in the frequency of listeriosis over time. In all analyses, we considered *P* values <.05 to be statistically significant. All reported *P* values are 2-tailed.

RESULTS

Epidemiology. Thirty *L. monocytogenes* infections were identified among 25,997 transplant recipients; infections were identified at 10 of the 15 participating hospitals. This figure represented 0.12% of all transplant recipients and included 14 (0.18%) of 7901 liver recipients, 8 (0.06%) of 12,390 kidney recipients, 4 (0.12%) of 3260 heart recipients, 2 (0.12%) of 1729 lung recipients, and 2 (0.29%) of 677 multivisceral re-

cipients. There were no cases of *Listeria* infection among 33 pancreas recipients and 7 small bowel recipients. No outbreak or cluster of cases of listeriosis occurred during the study period. No significant differences regarding the trend in the frequency of *Listeria* infection over time were observed ($P = .548$). The median time to diagnosis of listeriosis after transplantation was 202 days (range, 16–5189 days). Fifteen (50%) of the 30 case patients received a diagnosis of listeriosis >6 months after transplantation.

Risk factors for* Listeria *infection. The risk factors analyzed for the 30 case patients and 60 matched control subjects are shown in Table 1. On univariate analysis, diabetes mellitus, CMV infection or disease within the preceding 6 months, receipt of high-dose prednisone within the preceding 6 months, and the presence of allograft rejection within the preceding 6 months were significantly associated with listeriosis. There were 5 case patients with asymptomatic CMV infection and 3 case patients with CMV disease.

After applying a conditional logistic regression model (Table 2), diabetes mellitus (OR, 5.6; 95% CI, 1.6–19.6; $P = .007$), history of CMV infection or disease within the preceding 6 months (OR, 35.9; 95% CI, 2.1–620; $P = .014$), and receipt of high-dose prednisone within the preceding 6 months (OR, 6.2; 95% CI, 1.8–21.1; $P = .003$) were found to be independent risk factors for *Listeria* infection in SOT recipients, whereas TMP-SMZ prophylaxis at the time of event was found to be a protective factor (OR, 0.07; 95% CI, 0.006–0.76; $P = .029$).

Clinical characteristics of* Listeria *infection in SOT recipients. The clinical characteristics of the 30 SOT recipients with listeriosis are shown in Table 3. Seventeen patients (56.7%) were men, with a median age of 58.6 years. The median duration of symptoms prior to hospitalization was 3 days. Twenty-six patients (86.7%) had bacteremia, and 7 of these patients had septic shock at presentation. Other manifestations included meningoencephalitis, spontaneous peritonitis, pleural empyema, brain abscesses, and liver abscesses. As detailed in Table 3, 14 transplant recipients (46.7%) with listeriosis had ⩾1 coexisting infection, with the most common coexisting infection being CMV infection or disease. There was 1 case of late-onset CMV infection, which occurred 175 days after kidney transplantation.

Microbiology. *L. monocytogenes* was the species identified in all cases. The diagnosis of listeriosis was established with the use of 1 or more of the following methods: blood culture ($n = 26$), CSF culture ($n = 6$), ascitic fluid culture ($n = 2$), pleural fluid culture ($n = 1$), liver abscess purulent material

Table 1. Univariate Analysis of Risk Factors for *Listeria* Infection in Solid-Organ Transplant Recipients

Variable	Case patients ($n = 30$)	Control subjects ($n = 60$)	OR (95% CI)	*P*
Male sex	17 (56.7)	42 (70.0)	1.78 (0.72–4.43)	.21
Age, median years (range)	58.6 (32–75)	56.3 (21–73)	1.03 (0.99–1.08)	.10
Diabetes mellitus	15 (50.0)	9 (15.0)	5.67 (2.07–15.51)	<.001
Receipt of prior transplant	3 (10.0)	5 (8.3)	1.22 (0.27–5.49)	>.99
Multivisceral transplant	2 (6.7)	4 (6.7)	1.00 (0.17–5.79)	>.99
Receipt of prophylaxis with TMP-SMZ	3 (10.3)	12 (20.3)	0.45 (0.12–1.75)	.36
Receipt of antifungal prophylaxis	5 (17.2)	10 (16.9)	1.02 (0.31–3.32)	>.99
Receipt of CMV prophylaxis	2 (6.9)	3 (5.1)	1.38 (0.21–8.77)	>.99
CMV infection or disease within preceding 6 months	8 (26.7)	2 (3.3)	10.54 (2.08–53.57)	.002
Prednisone dose at the time of the event[a], median mg (range)	15 (2.5–45)	10 (1.25–75.0)	1.03 (0.99–1.08)	.159
Receipt of high-dose prednisone within preceding 6 months[b]	17 (58.6)	10 (18.2)	6.37 (2.33–17.46)	<.001
Elevated median calcineurin inhibitor level within preceding 30 days[c]	6 (20.0)	8 (13.3)	1.62 (0.51–5.20)	.538
Receipt of lymphocyte-depleting antibody within preceding 12 months	7 (24.1)	7 (12.7)	2.18 (0.68–6.98)	.223
Allograft rejection within preceding 6 months	13 (44.8)	8 (13.3)	5.28 (1.86–15.00)	.001
Lymphocyte count within preceding 30 days, median cells/mm^3 (range)	948 (110–3450)	1245 (153–3770)	1.00 (0.99–1.00)	.252
Neutrophil count within preceding 30 days, median cells/mm^3 (range)	4628 (1400–12,063)	4340 (500–17,935)	1.00 (1.00–1.00)	.799

NOTE. Data are no. (%) of patients, unless otherwise indicated. CI, confidence interval; CMV, cytomegalovirus; OR, odds ratio; TMP-SMZ, trimethoprim-sulfamethoxazole.

[a] Time of event was defined as the time of *Listeria* infection for the case patients and as the equivalent time for the matched control subjects.
[b] High-dose prednisone was defined as ⩾20 mg of prednisone for ⩾1 month or >2 pulses of 1 g intravenous methylprednisolone.
[c] Elevated median calcineurin inhibitor level was defined as >15 μg/mL for tacrolimus and >300 ng/mL for cyclosporine.

Table 2. Independent Risk Factors for *Listeria* Infection in Solid-Organ Transplant Recipients as Defined by Conditional Multivariable Logistic Regression

Variable	OR (95% CI)	*P*
Diabetes mellitus	5.6 (1.6–19.6)	.007
CMV disease or infection within preceding 6 months	35.9 (2.1–620)	.014
Receipt of high-dose prednisone within preceding 6 months[a]	6.2 (1.8–21.1)	.003
Receipt of TMP-SMZ prophylaxis	0.07 (0.006–0.76)	.029

NOTE. CI, confidence interval; CMV, cytomegalovirus; OR, odds ratio; TMP-SMZ, trimethoprim-sulfamethoxazole.

[a] High-dose prednisone was defined as ⩾20 mg of prednisone for ⩾1 month or >2 pulses of 1 g intravenous methylprednisolone. Variables included in the analysis were sex, age, diabetes mellitus, CMV disease or infection within the preceding 6 months, receipt of high-dose prednisone within the preceding 6 months, allograft rejection within the preceding 6 months, and receipt of TMP-SMZ prophylaxis at the time of the event.

culture ($n = 1$), and surgical specimen culture of brain abscess pus ($n = 1$). Serotypes and antimicrobial susceptibility were investigated in 13 *L. monocytogenes* isolates. The most frequent serotypes were 4 ($n = 9$) and 1 ($n = 4$). All strains were susceptible to ampicillin and TMP-SMZ.

Treatment and outcomes. As shown in Table 3, 28 patients (93.3%) were treated with ampicillin, and 11 of them were also given gentamicin. The initial intravenous treatment with ampicillin was switched to oral TMP-SMZ in 11 cases. Two liver transplant recipients presented with multiple brain and liver abscesses that required surgical and percutaneous drainage respectively. One heart transplant recipient had an acute episode of allograft rejection during treatment of listeriosis. Nine patients (30%) required intensive care unit admission, and 7 of them underwent mechanical ventilation. The median duration of antibiotic therapy was 21 days. Excluding patients who died, the median length of hospital stay was 30 days.

The 30-day mortality rate was 26.7% (8 of 30 patients died). The median time from diagnosis of listeriosis to death was 15 days (range, 6–29 days). Causes of death were sepsis ($n = 4$), multiorgan failure ($n = 2$), respiratory failure ($n = 1$), and neurological complications ($n = 1$). The 30-day mortality rate was statistically significantly higher among the 10 patients with meningoencephalitis than it was among the 20 case patients who presented with other manifestations (60% vs 10%; OR, 13.5; 95% CI, 1.99–93.25; $P = .007$). The 30-day mortality did not differ significantly between patients treated with ampicillin plus gentamicin and those who received antibiotic monotherapy (3 [27.3%] of 11 patients vs. 5 [26.3%] of 19 patients; OR, 1.05; 95% CI, 0.19–5.60; $P > .99$)

DISCUSSION

In recent years, the incidence of laboratory-confirmed invasive listeriosis in the general population in developed countries has decreased [14]. Surveillance programs have documented rates of infection ranging from 0.6 through 6.2 cases per million individuals [15]. The reported incidence of listeriosis among recipients of allogeneic blood and marrow transplants is much higher, ranging from 0.39% through 0.47% [16, 17]. To our knowledge, the frequency of listeriosis among recipients of a broad range of organ transplant types has not been evaluated. In the present multicenter study, the prevalence of sporadic listeriosis among SOT recipients was 0.12%. The prevalence was highest among the group of multivisceral recipients (0.29%), followed by liver transplant recipients (0.18%). This latter figure is similar to that encountered in a study reporting 1 case of listeriosis among 539 liver recipients (0.19%) at a single institution [5].

In our study, independent risk factors for *Listeria* infection in SOT recipients were diabetes mellitus, history of CMV infection or disease within the preceding 6 months, and receipt of high-dose prednisone within the preceding 6 months, whereas TMP-SMZ prophylaxis was a protective factor.

Several aspects of immunity, such as polymorphonuclear leukocyte function (ie, leukocyte adherence, chemotaxis, and phagocytosis) and bactericidal activity of serum are depressed in patients with diabetes mellitus [18, 19]. Consequently, certain specific infections are particularly common among these patients. Previous observational studies have suggested that diabetes mellitus may be a predisposing factor for developing listeriosis [3, 20]. Interestingly, experimental studies have also linked hyperglycemia to a greater susceptibility to *L. monocytogenes* infection [21]. In our study, 50% of recipients with listeriosis had diabetes mellitus, compared with 15% of control subjects. In recent years, posttransplant diabetes mellitus has emerged as a major adverse event associated with the receipt of immunosuppressive drugs [22, 23]. Therefore, developing strategies aimed to minimize this effect should be a focus of future research.

CMV infection may cause both invasive disease (ie, "direct effects") and a variety of secondary immune phenomena in transplant recipients [24–26]. The immunomodulatory effects of CMV are increasingly recognized, with previous reports associating CMV infection with other viral, bacterial, fungal, and

Table 3. Clinical Characteristics, Treatment, and Outcomes of 30 Solid-Organ Transplant Recipients with *Listeria* Infection

Variable	Patients
Male sex	17 (56.7)
Age, median years (range)	58.6 (32–75)
Transplant	
Liver	14 (46.7)
Kidney	8 (26.7)
Heart	4 (13.3)
Lung	2 (6.7)
Multivisceral	2 (6.7)
Temperature >38°C	25 (83.3)
Shock at presentation	7 (23.3)
Renal impairment[a]	17 (56.7)
Hypoalbuminemia[b]	21 (70.0)
Manifestations of *Listeria* infection	
Bacteremia	26 (86.7)
Meningoencephalitis	10 (33.3)
Spontaneous peritonitis	2 (6.7)
Pleural empyema	1 (3.3)
Liver abscesses	1 (3.3)
Brain abscesses	1 (3.3)
Coexisting infection	14 (46.7)
CMV infection or disease	7
Primary bacteremia	3
Extended-spectrum β-lactamase–producing *Klebsiella pneumoniae*	1
Staphylococcus epidermidis	1
Pseudomonas aeruginosa	1
Pulmonary infection	3
P. aeruginosa tracheobronquitis	1
Invasive pulmonary aspergillosis	1
Nosocomial pneumonia	1
Urinary tract infection	3
Enterococcus faecalis	1
Streptococcus agalactiae	1
Candida albicans	1
Herpes simplex virus stomatitis	1
ICU admission	9 (30.0)
Mechanical ventilation	7 (23.3)
Other complications	7 (23.3)
Seizures	2
Acute allograft rejection	1
Gastrointestinal bleeding	1
Congestive heart failure	1
Cholestasis	1
Hyponatremia	1
Antibiotic treatment	
Ampicillin	28 (93.3)
Gentamicin	11 (36.7)
TMP-SMZ	11 (36.7)
Length of intravenous antibiotic treatment, median days (range)[c]	21 (3–43)
Length of antibiotic treatment, median days (range)[c]	21 (7–56)
Length of hospitalization, median days (range)[c]	30 (7–210)
30-Day mortality	8 (26.7)

NOTE. Data are no. (%) of patients, unless otherwise indicated. CMV, cytomegalovirus; ICU, intensive care unit; TMP-SMZ, trimethoprim-sulfamethoxazole.

[a] Renal impairment was defined as a serum creatinine level >1.5 mg/dL.

[b] Hypoalbuminemia was defined as a serum albumin level <3 g/L.

[c] Patients who died were excluded from the analysis.

protozoan infections [27]. Interestingly, CMV disease has been associated with listeriosis in previous studies of blood and bone marrow transplantation [16]. Nevertheless, its role as an independent risk factor for listeriosis in SOT recipients has not been previously identified. Our data provide additional support for aggressive management of CMV disease to prevent the "indirect" effects of CMV infection.

Prednisone is a broad-acting immunosuppressant, affecting both the innate and adaptive immune responses. The use of steroids exerts a decisive influence on the immune function of macrophages and granulocytes, which are the main cell host defenses against bacteria. In our study, receipt of high-dose prednisone within the preceding 6 months was identified as an independent risk factor for listeriosis. The association of steroid use and *Listeria* infection has been well established in previous studies [6, 7, 28].

At present, SOT recipients are given TMP-SMZ for the first 6 months after transplantation for *Pneumocystis jirovecii* pneumonia prophylaxis in many centers. The routine use of TMP-SMZ has effectively eliminated this infectious complication [2, 29]. Nevertheless, in a recent study [30], TMP-SMZ prophylaxis was not shown to be protective against *Nocardia* infection. Given the excellent activity of TMP-SMZ against *L. monocytogenes* [31], some investigators have argued that its administration might help to prevent listeriosis. In fact, it has been hypothesized that the low prevalence of this infection among SOT recipients may be attributable to the use of TMP-SMZ [28, 32, 33]. However, no study has formally tested this assumption. Significantly, we found that TMP-SMZ prophylaxis is a protective factor for listeriosis. According to our data, 50% of cases of listeriosis in SOT recipients occur >6 months after transplantation. Therefore, extended prophylaxis should be carefully considered for patients at high risk of listeriosis (eg, those with diabetes mellitus, those who receive high-dose prednisone, and those who develop CMV infection or disease). Moreover, it should be borne in mind that nearly all cases of listeriosis are thought to be food-borne [34]. Therefore, all transplant recipients should be advised to avoid potentially contaminated foods, such as soft cheeses and unheated delicatessen meals. They should also be instructed regarding how to reduce the risk of infection by thorough cooking, avoidance of cross-contamination, and short-term refrigerated storage of perishable foods [35].

In this study, most of the SOT recipients with *L. monocytogenes* infection had bacteremia. Meningoencephalitis was also particularly common. Other less common manifestations were peritonitis, pleural empyema, liver abscesses, and brain abscesses. Other investigators have previously reported similar clinical manifestations of *L. monocytogenes* infection in transplant recipients [4, 7, 8, 9, 28].

One recent study found that listeriosis-related deaths among the general population decreased over the 16-year study period (1990–2005) [36]. In our study involving SOT recipients, both the 30-day and 1-year mortality rates were high (26.7% and 33.3%, respectively). The mortality was significantly higher among patients presenting with meningoencephalitis, reaching 60%. This finding corroborates those of previous reports [37–40]. Mizuno et al [37] described 1 case of listeriosis after liver transplantation and reviewed 14 previously reported cases. They found 4 cases of meningitis, with a mortality rate of 50%. Similarly, in a review of cases of listeriosis among renal transplant recipients, Stamm et al [38] found that the mortality rate was higher among patients with meningoencephalitis (37%) than it was among patients presenting with other manifestations (11%).

In conclusion, *L. monocytogenes* infection is uncommon among SOT recipients but causes high rates of morbidity and mortality, particularly among patients with meningoencephalitis. Independent risk factors for listeriosis are diabetes mellitus, CMV infection or disease, and receipt of high-dose steroids, whereas TMP-SMZ prophylaxis is a protective factor.

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References

1. Lorber B. Listeriosis. Clin Infect Dis **1997**; 24:1–9.
2. Fishman JA. Infection in solid-organ transplant recipients. N Engl J Med **2007**; 357:2601–14.
3. Skogberg K, Syrjänen J, Jahkola M, et al. Clinical presentation and outcome of listeriosis in patients with and without immunosuppressive therapy. Clin Infect Dis **1992**; 14:815–21.
4. Dee RR, Lorber B. Brain abscess due to *Listeria monocytogenes:* case report and literature review. Rev Infect Dis **1986**; 8:968–77.
5. Rettally CA, Speeg KV. Infection with *Listeria monocytogenes* following orthotopic liver transplantation: case report and review of the literature. Transplant Proc **2003**; 35:1485–7.
6. Zenati M, Milano A, Livi U, Cattelan A, Casarotto D. Successful treatment of disseminated infection with *Listeria monocytogenes* in a heart transplant recipient. J Heart Lung Transplant **1994**; 13:345–6.
7. Hristea I, Bunnapradist S, Peng A, Puliyanda D, Vo A, Jordan SC. The onset of rapidly progressive neurologic deterioration after a brief gastrointestinal illness in a renal allograft recipient. Transpl Infect Dis **2007**; 9:142–7.
8. Kruszyna T, Walsh M, Peltekian K, Molinari M. Early invasive *Listeria monocytogenes* infection after orthotopic liver transplantation: case report and review of the literature. Liver Transpl **2008**; 14:88–91.
9. Janssens W, Van Raemdonck D, Dupont L, Verleden GM. *Listeria* pleuritis 1 week after lung transplantation. J Heart Lung Transplant **2006**; 25:734–7.
10. Humar A, Michaels M, AST ID Working Group on Infectious Disease Monitoring. American Society of Transplantation recommendations for screening, monitoring and reporting of infectious complications in immunosuppression trials in recipients of organ transplantation. Am J Transplant **2006**; 6:262–74.

11. Murray PR, Baron EJ, Jorgensen JH, Landry ML, Pfaller MA. Manual of clinical microbiology. 9th ed. American Society for Microbiology. Washington, DC: Raven Press, **2007**.
12. NCCLS. Methods for antimicrobial dilution and disk susceptibility testing of infrequently isolated or fastidious bacteria; approved guideline. Clinical Laboratory Standards Institute document M45-A. Wayne, PA: NCCLS, **2006**.
13. Hosmer DW, Lemeshow S. Logistic regression: variable selection. In: Hosmer DW, Lemeshow S, eds. Applied logistic regression. 2nd ed. New York, NY: John Willey & Sons, **2000**.
14. Voetsch AC, Angulo FJ, Jones TF, et al. Centers for Disease Control and Prevention Emerging Infections Program Foodborne Diseases Active Surveillance Network Working Group. Reduction in the incidence of invasive listeriosis in foodborne diseases active surveillance network sites, 1996–2003. Clin Infect Dis **2007**; 44:513–20.
15. Bortolussi R. Listeriosis: a primer. CMAJ **2008**; 179:795–7.
16. Safdar A, Papadopoulous EB, Armstrong D. Listeriosis in recipients of allogeneic blood and marrow transplantation: thirteen year review of disease characteristics, treatment outcomes and a new association with human cytomegalovirus infection. Bone Marrow Transplant **2002**; 29: 913–6.
17. Chang J, Powles R, Mehta J, Paton N, Treleaven J, Jameson B. Listeriosis in bone marrow transplant recipients: incidence, clinical features, and treatment. Clin Infect Dis **1995**; 21:1289–90.
18. Delamaire M, Maugendre D, Moreno M, Le Goff MC, Allannic H, Genetet B. Impaired leucocyte functions in diabetic patients. Diabet Med **1997**; 14:29–34.
19. McMahon MM, Bistrian BR. Host defenses and susceptibility to infection in patients with diabetes mellitus. Infect Dis Clin North Am **1995**; 9:1–9.
20. Siegman-Igra Y, Levin R, Weinberger M, et al. *Listeria monocytogenes* infection in Israel and review of cases worldwide. Emerg Infect Dis **2002**; 8:305–10.
21. Ikejima S, Sasaki S, Sashinami H, et al. Impairment of host resistance to *Listeria monocytogenes* infection in liver of db/db and ob/ob mice. Diabetes **2005**; 54:182–9.
22. Araki M, Flechner SM, Ismail HR, et al. Posttransplant diabetes mellitus in kidney transplant recipients receiving calcineurin or mTOR inhibitor drugs. Transplantation **2006**; 81:335–41.
23. Penfornis A, Kury-Paulin S. Immunosuppressive drug-induced diabetes. Diabetes Metab **2006**; 32:539–46.
24. Razonable RR. Cytomegalovirus infection after liver transplantation: current concepts and challenges. World J Gastroenterol **2008**; 14: 4849–60.
25. Singh N. Cytomegalovirus infection in solid organ transplant recipients: new challenges and their implications for preventive strategies. J Clin Virol **2006**; 35:474–7.
26. Meylan PR, Manuel O. Late-onset cytomegalovirus disease in patients with solid organ transplant. Curr Opin Infect Dis **2007**; 20:412–8.
27. Pérez-Sola MJ, Castón JJ, Solana R, Rivero A, Torre-Cisneros J. Indirect effects of cytomegalovirus infection in solid organ transplant recipients. Enferm Infecc Microbiol Clin **2008**; 26:38–47.
28. Eckburg PB, Montoya JG, Vosti KL. Brain abscess due to *Listeria monocytogenes*: five cases and a review of the literature. Medicine (Baltimore) **2001**; 80:223–35.
29. Fishman JA. Prevention of infection caused by *Pneumocystis carinii* in transplant recipients. Clin Infect Dis **2001**; 33:1397–405.
30. Peleg AY, Husain S, Qureshi ZA, et al. Risk factors, clinical characteristics, and outcome of *Nocardia* infection in organ transplant recipients: a matched case-control study. Clin Infect Dis **2007**; 44:1307–14.
31. Spitzer PG, Hammer SM, Karchmer AW. Treatment of *Listeria monocytogenes* infection with trimethoprim-sulfamethoxazole: case report and review of the literature. Rev Infect Dis **1986**; 8:427–30.
32. del Pozo JL. Update and actual trends on bacterial infections following liver transplantation. World J Gastroenterol **2008**; 14:4977–83.
33. Muñoz P, Muñoz RM, Palomo J, Rodríguez-Creixems M, Muñoz R, Bouza E. *Pneumocystis carinii* infection in heart transplant recipients: efficacy of a weekend prophylaxis schedule. Medicine (Baltimore) **1997**; 76:415–22.
34. Mead PS, Slutsker L, Dietz V, et al. Food-related illness and death in the United States. Emerg Infect Dis **1999**; 5:607–25.
35. Goulet V. What can we do to prevent listeriosis in 2006? Clin Infect Dis **2007**; 44:529–30.
36. Bennion JR, Sorvillo F, Wise ME, Krishna S, Mascola L. Decreasing listeriosis mortality in the United States, 1990–2005. Clin Infect Dis **2008**; 47:867–74.
37. Mizuno S, Zendejas IR, Reed AI, et al. *Listeria monocytogenes* following orthotopic liver transplantation: central nervous system involvement and review of the literature. World J Gastroenterol **2007**; 13: 4391–3.
38. Stamm AM, Dismukes WE, Simmons BP, et al. Listeriosis in renal transplant recipients: report of an outbreak and review of 102 cases. Rev Infect Dis **1982**; 4:665–82.
39. Clauss HE, Lorber B. Central nervous system infection with *Listeria monocytogenes*. Curr Infect Dis Rep **2008**; 10:300–6.
40. Brouwer MC, van de Beek D, Heckenberg SG, Spanjaard L, de Gans J. Community-acquired *Listeria monocytogenes* meningitis in adults. Clin Infect Dis **2006**; 43:1233–8.