Transplantation Reports 4 (2019) 100022

Contents lists available at ScienceDirect

Transplantation Reports

journal homepage: www.elsevier.com/locate/tpr

Evaluation of the first liver transplantations in our transplant center experience

Muhammed Rasid Aykota[a,*], Tugba Sari[b], Sevda Yilmaz[a], Asli Mete[c], Erdem Carti[d], Ali Kagan Gokakin[a]

[a] Department of General Surgery, Pamukkale University Faculty of Medicine, Denizli, Turkey
[b] Department of Infectious Diseases and Clinical Microbiology, Pamukkale University Faculty of Medicine, Denizli, Turkey
[c] Department of Anestesiology, Pamukkale University Faculty of Medicine, Denizli, Turkey
[d] Department of General Surgery, Adnan Menderes University Faculty of Medicine, Aydın, Turkey

ARTICLE INFO

Keywords:
Liver
Transplantation
Transplant center

ABSTRACT

Purpose: Orthotopic liver transplantation is life-saving in patients with end-stage liver failure. However, infections and acute rejection are the most important causes of morbidity and mortality. Liver transplantation in the treatment of liver failure has begun to be implemented for the first time in Pamukkale University Medical Faculty Health Research and Training Hospital, and the results of liver transplants are shared in this report.
Material and method: A total of five cadaveric donor liver transplantation cases were evaluated prospectively. Patients' demografic findings and infectious complications detected after transplantation were examined.
Findings: Two of the patients was male, three were female. The mean age was 57.8 ± 9.9 years and the mean MELD score was 12.8 ± 2.4. The organisms isolated included *Escherichia coli, Acinetobacter baumannii* and *Pseudomonas aeruginosa*. Two patients' had blood stream infection with urinary tract infection (UTI) and one patients' had postoperative wound infection after bilary leakage. One patients' developed pneumonia. One patient was developed tacrolimus-induced severe persistent diarrhea and recovered thereafter reduced tacrolimus dose. One of the patients died of post-op 3 days because of reperfusion syndrome.
Conclusion: New liver transplantation practices in our country will make many diseases that cause liver failure become treatable as in our transplant center. The duration of hospital stay, intensive care unit stay, invasive interventions, blood transfusions, immunosuppressive treatments cause an increased risk of infection in these patients and high mortality is seen despite antibiotic treatment.

1. Purpose

Orthotopic liver transplantation is life-saving in patients with end-stage liver failure. Despite surgical advances and effective prophylactic strategies in liver transplant, infections and acute rejection are a significant source of posttransplantation morbidity and mortality [1–3].

Most infectious complications (up to 80% of liver recipients) occur during the first year after liver transplant [4]. The overwhelming majority of early infections after transplantation are health care associated bacterial infections. Opportunistic infections such classically occur 1 to 6 months. After 6 months remain at increased risk for typical community-acquired bacterial and viral infections [4].

These infections' diagnosis and treatment are often delayed because immunosuppressive therapy diminishes inflammatory responses [1,2]. Infections must be identified early enough and treated properly. In addition, prophylactic approaches remain controversial [1,2,5]. Liver transplantation in the treatment of liver failure has begun to be implemented for the first time in Pamukkale University Medical Faculty Health Research and Training Hospital. Our aim was to review our early postoperative infection management after liver transplant.

2. Material and method

A total of five cadaveric donor liver transplantation cases were

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; APACHE, acute physiology and chronic health evaluation; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HT, hypertension; MELD, model for end stage liver disease; NASH, non alcoholic stetaohepatitis; UTI, urinary tract infection

* Corresponding author at: Department of General Surgery, Pamukkale University Faculty of Medicine, Denizli, Turkey.
E-mail address: muhammedaykota@hotmail.com (M.R. Aykota).

https://doi.org/10.1016/j.tpr.2019.100022
Received 22 November 2018; Accepted 10 April 2019
Available online 12 April 2019

Table 1
Demographic and clinical characteristics of liver transplant patients.

Patient Characteristics	Case 1	Case 2	Case 3	Case 4	Case 5
Sex/age	Female/42	Female /63	Male/65	Female /54	Male/65
MELD	17	12	11	13	11
Child-Pugh A B C	12 C	9 B	10 B	8 B	6B
Endication	NASH	NASH	Cryptogenic liver cirrhosis	NASH	Hepatitis b liver cirrhosis, hepatocellular carcinomatosis
Comorbid diseases	DM + HT	DM + HT + CAD	DM	DM + HT	COPD
Donor charecterization	Cadaveric	Cadaveric	Cadaveric	Cadaveric	Cadaveric
Operation time / hour	7	6	8	7	8
Reoperation/postop. day	None	Femur fracture/postop 82. day Biliary leakage /postop 94. day	Hepatic artery thrombosis /postop 1.day	None	None
Blood transfusion (U)	16	2	8	17	10
Hospitalization day	10	9	10	28	37
Intensive care unit stay day	1	1	1	2	2
Postop infections/day	Pneumonia/postop 2.day	Postoperative wound infection/ post op 120. day UTI/post op 132. day Blood stream infection/post op 132. day	None	None	UTI, Blood stream infection/ postop 19.day
ALT/AST (mg/dL) levels during infection	475/219	10/9			29/26
WBC (K/uL) level during infection	7840	19,980			15,650
CRP (mg/dL) level during infection	6.7	37.5			3.5
Tacrolimus level during infection	4.3	10.7			8,29
Antibiotic regimen	Piperacillin tazobactam	Imipenem + fosfomycin + tigecycline			Meropenem
Clavien Dindo classification	2	3b	3b	5	2
Survey	Cure	Cure	Cure	Exitus	Cure

MELD: Model for end stage liver disease, NASH: Non alcoholic stetaohepatitis, DM:Diabetes mellitus, HT: Hypertension, CAD: Coronary artery disease, COPD: Chronic obstructive pulmonary disease, UTI: urinary tract infection.

evaluated prospectively. Patients' sex, etiology of liver failure, Child and MELD score, blood transfusions, hospital stay, and infectious complications detected after transplantation were examined. Infections were grouped as surgical site and nonsurgical site infections. Consequences and treatment protocols of infections were stratified according to the Clavien scale. Surgical prophylaxis was performed for a maximum of 48 h. All of the trimethoprim/sulfamethoxazole and valgancyclovir profilaxis were initiated within the first 10 days after transplantation. The standard immunosuppressive treatment protocol was identified as is tacrolimus, mycophenolatmofetil and methyl prednisolone for the first three months after transplantation. All liver transplant recipients were tested for latent tuberculosis, syphilis, hepatitis A, hepatitis B, hepatitis C, human immunodeficiency virus, Epstein-Barr virus and cytomegalovirus.

3. Findings

Two of the patients was male, three were female. Between December 2017 and November 2018, we performed 5 liver transplants at our center (patient age range, 42 to 65 years), which included 5 deceased donor (100%) liver transplants. Early postoperative nonsurgical site infections were detected in three patients (60%). No mortalities occurred in patients with infections. One patient died of post-op 3 days because of reperfusion syndrome. The demographic, laboratory and clinical characteristics of the patients are presented in Table 1. The mean age was 57.8 ± 9.9 years and the mean MELD score was 12.8 ± 2.4. The mean duration of hospital stay of the patients was 18.8 ± 12.9 days with a mean intensive care unit stay of 1.4 ± 0.5 days. ALT (alanine aminotransferase), AST (aspartate aminotransferase) and the mean level of serum total bilirubin higher levels were found on first post operation day. ALT and AST levels were decreased sharply during the next five days and declined to normal on day 15 post operation but serum total bilirubin levels progressively improved until stabilizing in the normal range by the end of the first month. The mean albumin, PT, APTT and INR were 2.1 mg/dL, 18, 44 and 2.8 s, respectively.

Two patients' had blood stream infection with urinary tract infection (UTI) and one patients' had postoperative wound infection after bilary leakage. One patients' developed pneumonia. One patients' developed tacrolimus-induced severe persistent diarrhea and recovered thereafter reduced tacrolimus dose. One patients' developed hepatic trombosis one day after transplant and requiredre-operation. The organisms isolated included *Escherichia coli, Acinetobacter baumannii* and *Pseudomonas aeruginosa*.

4. Conclusion

New liver transplantation practices in our country will make many diseases that cause liver failure become treatable as in our transplant center. Like any young program, our transplant program continue to grow. Policies, lists, reports, and benchmarks were created to increase efficiency by streamlining a review process, which resulted in consistent and cost-effective operations as well as improved patient care. Cases are periodically reviewed to ensure that the benefits of a transplant outweigh the risks, resulting in improved overall outcomes.

Significant infections that required therapy in the perioperative period despite antibacterial prophylaxis were seen in 3 of our patients. Infections are the principal complications in liver transplant recipients, occurring in 60–70% of cases [2,6] A recent study reported that serious infectious complications occurred in 52% of the patients within 15 months and 57% of these were bacterial infections that occurred in the first month after transplant [7].

One of our patients' had pneumonia but there was not found causative microorganism. Posttransplant pneumonia in the first 100 days incidence has been described to vary from 5% to 48% and manifested as the need for prolonged use of mechanical ventilation, extended stay in the intensive care unit, and the need for a tracheotomy, among other complications [8–11]. Gram-negative bacilli are the predominant microorganisms involved in posttransplant pneumonia, accounting for up to 84% [8–13].

Two of the our patients' had blood stream infection and had similarly risk factors like reported in the literature. Bloodstream infection has been known as a major determinant for morbidity and mortality in liver transplant recipients [14–17]. Risk factors for developing blood stream infection include severity of liver diseases, comorbidities, massive pleural effusion or ascites requiring drainage, diabetes mellitus, low serum albumin level, older donor or recipient age and ABO incompatibility [15,17–19] Similarly, operative blood loss, positive bile culture, re-operation, cytomegalovirus infection, higher acute physiology and chronic health evaluation (APACHE) II score after surgery and longer catheterization have been reported as intraoperative or postoperative risk factors [14,16,19].

Two of the our patients' had UTI which is a common complication after liver transplant, and two-thirds of UTI episodes in recipients occur during the first month after transplant (20). Risk factors for developing UTI include; female sex, hospitalization 2 to 7 days before transplant, frequency of abdominal exploration, and high body mass index, mycophenolate mofetil or antithymocyte globulin use, need for immediate posttransplant dialysis, diabetes mellitus, number of episodes of acute graft rejection, length of hospitalization, duration of Foley catheterization, number of episodes of acute rejection, and increase in immunosuppression (21) Gram-negative bacteria were the most common causative agents of post-liver transplant infection (63.3%; *E. coli* 30.4%), followed by gram-positive bacteria (comprising 25.3%) and fungi (11.4%) (22–25). *A. baumannii* and extended-spectrum beta-lactamase-positive *E. coli* were identified in our patient's urine culture.

The incidence of biliary complications is 5% to 30% after orthotopic liver transplantation [20,21] Biliary leakage occurs in 7.8% of cases, mainly in the early postoperative period [22]. Nosaka et al. [23]. reported a clear association between biliary leaks and opportunistic infection with Enterobacter species in experimental liver transplantation in rats and reported that potential role of infection in the obviation of arterial collateralization, causing bile duct necrosis and subsequent biliary leaks. In our case, *A. baumannii* growth was detected in the abdominal fluid sample taken after bile leakage.

Initiation of appropriate prophylactic and therapeutic protocols at the right time decreases morbidity and mortality due to infection in liver transplant recipients. Increased understanding and effective approaches to prevent infection are essential to improving recipient survival. The duration of hospital stay, intensive care unit stay, invasive interventions, blood transfusions, immunosuppressive treatments cause an increased risk of infection in these patients and high mortality is seen despite antibiotic treatment.

Funding

None.

References

[1] E.H. Ayvazoglu Soy, A. Akdur, S. Yildirim, H. Arslan, M. Haberal, Early postoperative infections after liver transplant, Exp. Clin. Transplant. Off. J. Middle East Soc. Organ Transplant. 16 (Suppl 1) (Mar. 2018) 145–148 Suppl 1.
[2] J.E. Kim, et al., Infections after living donor liver transplantation in children, J. Korean Med. Sci. 25 (4) (Apr. 2010) 527–531.
[3] G. Immordino, et al., Predictability and survival in liver replantransplantation: monocentric experience, Transplant. Proc. 46 (7) (Sep. 2014) 2290–2292.
[4] G. Patel, S. Huprikar, Infectious complications after orthotopic liver transplantation, Semin. Respir. Crit. Care Med. 33 (01) (Feb. 2012) 111–124.
[5] European Association for the Study of the Liver, EASL clinical practice guidelines: liver transplantation, J. Hepatol. 64 (2) (2016) 433–485.
[6] A. Jain, et al., Pediatric liver transplantation. A single center experience spanning 20 years, Transplantation 73 (6) (Mar. 2002) 941–947.
[7] R.W. Shepherd, et al., Risk factors for rejection and infection in pediatric liver transplantation, Am. J. Transplant. Off. J. Am. Soc. Transplant. Am. Soc. Transpl.

Surg. 8 (Feb. (2)) (2008) 396–403.
[8] J. Prieto Amorin, M. Lopez, K. Rando, J. Castelli, J. Medina Presentado, Early bacterial pneumonia after hepatic transplantation: epidemiologic profile, Transplant. Proc. 50 (Mar. (2)) (2018) 503–508.
[9] P. Feltracco, C. Carollo, S. Barbieri, T. Pettenuzzo, C. Ori, Early respiratory complications after liver transplantation, World J. Gastroenterol. 19 (Dec. (48)) (2013) 9271–9281.
[10] D. Xia, et al., Postoperative severe pneumonia in adult liver transplant recipients, Transplant. Proc. 38 (Nov. (9)) (2006) 2974–2978.
[11] C. Aydin, et al., Postoperative pulmonary complications after liver transplantation: assessment of risk factors for mortality, Transplant. Proc. 47 (Jun. (5)) (2015) 1488–1494.
[12] A. De Gasperi, P. Feltracco, E. Ceravola, E. Mazza, Pulmonary complications in patients receiving a solid-organ transplant, Curr. Opin. Crit. Care 20 (Aug. (4)) (2014) 411–419.
[13] A. Pirat, S. Ozgur, A. Torgay, S. Candan, P. Zeyneloğlu, G. Arslan, Risk factors for postoperative respiratory complications in adult liver transplant recipients, Transplant. Proc. 36 (Feb. (1)) (2004) 218–220.
[14] C.J. Karvellas, et al., Bloodstream infection after elective liver transplantation is associated with increased mortality in patients with cirrhosis, J. Crit. Care 26 (Oct. (5)) (2011) 468–474.
[15] F. Bert, et al., Microbial epidemiology and outcome of bloodstream infections in liver transplant recipients: an analysis of 259 episodes, Liver Transplant. Off. Publ. Am. Assoc. Study Liver Dis. Int. Liver Transplant. Soc. 16 (Mar. (3)) (2010) 393–401.
[16] T. Iida, et al., Posttransplant bacteremia in adult living donor liver transplant recipients, Liver Transplant. Off. Publ. Am. Assoc. Study Liver Dis. Int. Liver Transplant. Soc. 16 (Dec. (12)) (2010) 1379–1385.
[17] N. Singh, D.L. Paterson, T. Gayowski, M.M. Wagener, I.R. Marino, Predicting bacteremia and bacteremic mortality in liver transplant recipients, Liver Transplant. Off. Publ. Am. Assoc. Study Liver Dis. Int. Liver Transplant. Soc. 6 (Jan. (1)) (2000) 54–61.
[18] M. Hashimoto, et al., Bloodstream infection after living donor liver transplantation, Scand. J. Infect. Dis. 40 (6–7) (2008) 509–516.
[19] S.I. Kim, et al., Epidemiology and risk factors for bacteremia in 144 consecutive living-donor liver transplant recipients, Yonsei Med. J. 50 (Feb. (1)) (2009) 112–121.
[20] M. Gastaca, Biliary complications after orthotopic liver transplantation: a review of incidence and risk factors, Transplant. Proc. 44 (Aug. (6)) (2012) 1545–1549.
[21] H. Salahi, et al., Biliary tract complications after liver transplantation in a single center, Transplant. Proc. 37 (Sep. (7)) (2005) 3177–3178.
[22] N. Akamatsu, Y. Sugawara, D. Hashimoto, Biliary reconstruction, its complications and management of biliary complications after adult liver transplantation: a systematic review of the incidence, risk factors and outcome, Transpl. Int. Off. J. Eur. Soc. Organ Transplant. 24 (Apr. (4)) (2011) 379–392.
[23] T. Nosaka, J.L. Bowers, O. Cay, M.E. Clouse, Biliary complications after orthotopic liver transplantation in rats, Surg. Today 29 (9) (1999) 963–965.