

## Liver allografts from donors with peritoneal contamination: report of two cases

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### ABSTRACT

Organs from deceased donors with traumatic abdominal injury, peritoneal contamination and open abdomen are usually discarded due to risks of transmission of severe infections to the recipient. There are no specific recommendations regarding organ utilization from these donors, but they might be an unexplored source able to attenuate organ shortage. Herein, the first successful report of a case involving liver transplantation using a liver allograft procured from a deceased donor with an open abdomen is outlined. This donor was a young trauma patient in which peritoneal contamination had occurred following a gunshot wound. Also included in this the report is liver transplant from a donor, who also was a trauma victim with an enteric perforation. The decision-making process to accept liver allografts from donors with a greater risk of peritoneal infection involved the absence of uncontrolled sepsis or visible contamination of the cavity. Appropriate donor-recipient matching and adequate anti-infectious management might have contributed to a favorable outcome, which suggest that these donors can be used as alternatives to reduce organ shortage.

**Key words.** Liver transplantation. Deceased donors. Open abdomen. Peritoneal contamination. Trauma patients.

### INTRODUCTION

There is an increasing gap between organ demand for transplantation and donor supply. In order to accommodate the growing waiting list, the transplant community has increased efforts to expand the donor pool by utilization of donors with expanded criteria, which may also include those with documented active infection.<sup>1</sup> However, there is a scarcity of information about the safety use of grafts from donors who suffered penetrating abdominal trauma including the ones whose abdominal wall was kept opened.

The presence of bacteremia in the donor has been proven to have no impact on recipient survival

as long as adequate antimicrobial treatment has been provided.<sup>2</sup> However, information regarding the use of organs from donors with peritoneal contamination is scarce, and only one prior case report described the outcomes of recipients who were transplanted using organs from a donor with an open abdomen.<sup>3</sup> Although two of the recipients of the organs from this donor had a good outcome, the liver transplant recipient died during in-hospital stay. Herein, two cases of patients who underwent liver transplantation receiving allografts procured from trauma victims in which peritoneal cavity had been exposed to an important degree of contamination, including one who had an open abdomen are presented.

### CASE REPORT

#### Case 1: donor with an open abdomen and abdominal packing

A 24-year-old male with traumatic brain, abdominal, and thoracic injuries underwent laparotomy

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*Manuscript received: August 12, 2014.*  
*Manuscript accepted: September 16, 2014.*

with splenectomy, abdominal packing, and vacuum dressing. Antibiotic coverage with cefepime and vancomycin was initiated for suspected sepsis on the fourth postoperative day (POD). Brain death was declared on the sixth POD, and the following laboratory findings were obtained:

- Hb = 9.6g/dL.
- Leukocytes = 39.810/mm<sup>3</sup>, with 13% bands.
- Platelets = 29,000 mm<sup>3</sup>.
- Na<sup>+</sup> = 158 mg/dL.
- pH = 7.41.
- PaO<sub>2</sub> = 177 mmHg.
- Total bilirubin = 1.4 mg/dL.
- Direct bilirubin = 0.5 mg/dL.
- AST = 58 U/L.
- ALT = 60 U/L.
- Alkaline phosphatase = 102 U/L.
- Lipase = 28 U/L.

Peripheral perfusion was normal and mean arterial pressure (MAP) was maintained at about 70 mmHg by a norepinephrine dose of 0.01 µg/kg/min. During procurement operation, abdominal packing was carefully removed and abdominal cavity inspection revealed superficial lacerations on the liver and a small amount of dark blood on paracolic gutters and pelvis. Peripheral blood, preservation solution, airway secretion, and urine, as well as swabs from peritoneal cavity and peritoneal lavage were sampled for microbiological analysis. Liver biopsy revealed normal architecture, without cell infiltrates. The liver was transplanted into a 54-year-old male recipient with hepatitis C virus-related cirrhosis, a 6 cm hepatocellular carcinoma, and a calculated Model of End-Stage Liver Disease (MELD) score of 11. Cold ischemia time was 504 min. On POD 1, Gram stain from the peritoneal lavage was positive for gram-negative rods, and thus antibiotic treatment with piperacillin-tazobactam was maintained. On POD 3, body temperature was 37.5 °C and mild leukocytosis, without hemodynamic instability occurred. *Serratia marcescens* resistant only to doxycycline, but sensitive to cephalosporins and other combinations of penicillins grew from peritoneal lavage (peritoneal fluid obtained from donor's peritoneal cavity after instillation of saline). The recipients thus presented with subfebrile peaks associated to mild leukocytosis until POD 5, but improved with no further intervention. Serial blood cultures were all negative. Antibiotics were discontinued on POD 7. Tacrolimus was initiated on POD 3 and maintained on a low trough on the first post-trans-

plant week. A biopsy-proven mild acute cellular rejection was detected on POD 9, and responded to increased immunosuppression without steroid bolus. The recipient was discharged with normal liver serum tests on POD 25. He was alive with no signs of infection or disease recurrence one year after transplant.

### Case 2:

#### donor with penetrating abdominal trauma

A 22-year-old male donor who sustained multiple gunshot wounds to his skull, left thigh and abdomen underwent laparotomy. Sutures were performed on involved organs (small bowel and bladder), and the midline incision was closed with a running suture. Right-sided pneumonia was diagnosed on POD 2, and antibiotic coverage with cefepime was started. Brain death was declared on day 3, and the following laboratory findings were obtained:

- Hb: 6.7 g/dL.
- Leukocytes: 14.740 mm<sup>3</sup>; 9% bands.
- Platelets: 82,000 mm<sup>3</sup>.
- Na<sup>+</sup>: 165 mg/dL.
- pH: 7.35.
- PO<sub>2</sub>: 266 mmHg.
- Total bilirubin: 1.3 mg/dL.
- Direct bilirubin: 0.6 mg/dL.
- AST: 70 U/L.
- ALT: 43 U/L.
- Lipase: 11 U/L.

Chest radiograph revealed a consolidation in the middle third of the right lung. Peripheral perfusion was normal and MAP was maintained at 65 mmHg without vasopressors. On procurement, liver macroscopy was normal, and there was no contamination in the cavity. Liver biopsy revealed minimal sinusoidal congestion. Blood, peritoneal lavage, airway secretion, urine and preservation solution fluid were sampled for microbiological analysis. The liver was transplanted into a 58-year-old female recipient with hepatitis C virus-related cirrhosis and a 5 cm hepatocellular carcinoma. There was no evidence of uncontrolled sepsis in the donor. Thus, cefepime was kept, and vancomycin was introduced to broaden the antimicrobial spectrum. Cold ischemia time was 430 min, with no occurrence of postoperative clinical and/or laboratory signs of graft dysfunction. On POD 1, Gram stain from peritoneal lavage was positive for gram-negative rods. On POD 3, three organisms were isolated from donor peritoneal

lavage: coagulase-negative *Staphylococcus* resistant to oxacillin and sensitive to vancomycin, *Klebsiella pneumoniae* resistant only to trimethoprim/sulfamethoxazole, and *Enterococcus faecium* resistant to vancomycin, teicoplanin, ampicillin, and only sensitive to aminoglycosides. In spite of the antibiogram findings, aminoglycosides were not introduced because patient was presenting with an uneventful recovery. Immunosuppressive strategy was the same as used in the previous case. The recipient was discharged on POD 22. She had normal graft function and no evidence of infection, disease, or tumor recurrence one year after transplant.

## DISCUSSION

The use of suboptimal donors is an expanding practice utilized for fulfilling the disparity between organ supply and demand. Although the use of organs from donors suffering from extra abdominal infections is a current practice, the presence of active abdominal infection is still considered a contraindication for organ utilization. In this setting, trauma victims with peritoneal contamination are rarely considered as suitable donors. In such instances, risks for donor-recipient infection transmissions have not yet been established. Optimal anti-infectious management plays a decisive role in decreasing the risk of infection transmission.<sup>4</sup> This includes collecting cultures from all sources and starting the recipients on preemptive antibiotic coverage.

Despite the potential for infectious transmissions that may lead to recipient death, our liver transplant program has decided to consider all abdominal trauma victims with limited peritoneal contamination as potential candidates for liver donation. To the best of our knowledge, this is the first report of procurement and successful liver transplantation using a liver allograft from a deceased donor with an "open abdomen". Successful evidence of the use of a liver allograft from a deceased donor with a gunshot to the abdomen resulting in intestinal perforation that had been sewn also is presented in this report.

Bacteremia occurs in about 5% of the organ donors.<sup>2,5</sup> Although it has been recently reported that donor-derived bacteremia may occur despite antibiotic prophylaxis,<sup>6</sup> infectious transmission can usually be avoided when an adequate antibiotic regimen is provided to the recipient.<sup>5,7</sup> In our experience, besides providing antibacterial treatment to the donor and also to the recipient, there must be an absence of uncontrolled systemic infection and visible perito-

neal contamination. Although there were no signs of peritonitis, microorganisms were isolated from cultures obtained from peritoneal cavity in both cases. Nevertheless, no evidence of donor-related infection was detected in the recipients, suggesting that low amounts of inoculum may not be enough to trigger sepsis. For example, contaminations of preservation solution carry low risk of causing recipient sepsis and may not jeopardize recipient outcomes.<sup>8,9</sup> This reinforces the concept that as long as preemptive antibacterial treatment is provided to the recipient, the presence of limited bacterial transmission may not be deleterious to recipient outcomes. This concept is also corroborated by the fact that individuals with traumatic colonic injuries, in which contamination is nearly universal, primary repair has been advocated by several authors, with lower complication rates than two-stage surgery.<sup>10,11</sup>

Although cultures obtained from the donors did not change the antibiotic therapy used in our cases, we consider collecting donor samples for microbiological analysis in this specific scenario in order to guide further adjustments in the antibiotic therapy of utmost importance. In the only previous report in which a patient with an "open abdomen" was used as a multiple organ donor, a multidrug-resistant *Pseudomonas aeruginosa* was isolated in postoperative cultures obtained from kidney, heart, and liver recipients. According to this report, there were two postoperative deaths, apparently not caused by donor-derived infections. However, a virulent organism (multidrug-resistant *Pseudomonas aeruginosa*) was identified in all four organ recipients, including the liver recipient who did not survive. Detection of this virulent organism allowed for the tailoring of antimicrobial therapy for the other recipients.

We recommend that a conservative approach should be taken when accepting organs from donors in which abdominal cavity has been recently violated. The key point on evaluating donors with peritoneal contamination would be to discriminating between contamination of the peritoneal cavity and infectious peritonitis. A similar concept is utilized in lung transplantation, in which organs with contamination of the airways may be utilized, but organs with parenchymal infection (pneumonia) are usually discarded.<sup>12</sup>

Although organs from bacteremic donors have been used successfully, such expansion of the donor pool requires consideration of the infectious risk associated with suboptimal donors.<sup>13</sup> In such instances, consulting with local infectious diseases service may be helpful for tailoring the most appropriate

empirical bacterial coverage based on each specific local infectious epidemiology. Although a recent study showed that liver recipients might be more vulnerable to donor-derived bacteremia, the presence of infection had no significant impact on outcomes, suggesting that livers from bacteremic donors can be utilized safely for transplantation.<sup>14</sup> The presence of bacteremia by multidrug-resistant agents seems to impose higher risks of severe donor-derived sepsis and death.<sup>3</sup> We believe that patients with an “open abdomen” and unequivocal signs of gross peritonitis or bacteremia associated to an “open abdomen” should not be considered as potential liver donors, especially those with bacteremia caused by multidrug-resistant agents.

As occurs with most marginal liver donors, careful selection associated to donor-recipient matching is crucial to achieving favorable outcomes in this setting. As was performed in the cases presented herein, we believe that liver allografts from patients with peritoneal colonization should be matched to recipients with preserved cardiopulmonary and renal function, since critically ill patients are usually more vulnerable to any amount of contamination. It is not our practice to transplant patients with a calculated MELD below 15, but the recipients included here had high appeal scores based on the presence of hepatocellular carcinoma. In addition, it is important to select young donors and avoid prolonged cold and warm ischemia times. Poor initial graft function may act as a trigger for uncontrolled sepsis.

In conclusion, these cases illustrate the benefits and the rationale of proactive strategy towards utilization of suboptimal grafts from donors with contamination of the abdominal cavity. The incidence of abdominal trauma victims with brain death is especially high in developing countries. The use of such patients as organ donors may help to expand the pool of organs for transplant. Additional data are necessary to demonstrate whether these organs should be used on a larger scale. Meanwhile, the decision to accept organs from these donors should be made on a case-by-case basis and in accordance to each specific transplant program policy with further consideration to donor availability in a particular region.

## ABBREVIATIONS

- **MAP:** mean arterial pressure.
- **MELD:** Model of End-Stage Liver Disease.
- **POD:** postoperative day.

## ACKNOWLEDGMENT

The authors thank Ms. Jessica J. Murphy for grammatical review.

## DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose.

## FUNDING

This study was not supported by any funding.

## AUTHORSHIP

TJMGF participated in research design, collecting the research data, and writing of the manuscript; ADC, IL, MFC, CDPK and CRPK participated in research design, and writing of the manuscript.

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