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Case report

Organ transplantation from a donor colonized with a multidrug-resistant organism: a case report

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Abstract: The number of intensive care unit patients with infections caused by multidrug-resistant organisms is increasing in most developed countries. We report the case of a deceased multiorgan donor, who was an asymptomatic carrier of carbapenem-resistant *Klebsiella pneumoniae* (CR-KP) in the respiratory tract, a condition that was not diagnosed before organ harvesting and transplantation. The outcome of the 2 kidney recipients, the liver recipient, and 1 of the lung recipients was uneventful; in particular, no evidence of infection transmission or adverse graft outcomes was noted. The other lung recipient had a complicated postoperative course and, 4 weeks post transplantation, he developed a bacteremic pneumonia with CR-KP from which he subsequently died. These results suggest that, in well defined conditions, organs from donors who are CR-KP positive may be considered for transplantation.

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A significant and increasing gap exists between the number of patients waiting for organ transplantation and the number of available organs. For this reason, it remains essential that maximum use be made of every available organ donor, while not endangering the recipient.

The presence of donor infections and possible transmission to the recipient is a condition that may potentially impact on recipient outcomes. In this regard, it has been estimated that 5% of organ donors have bacteremia at the time of organ procurement (1). This may be related to the use of medical devices commonly employed in donor management, such as urinary and central venous catheters, resulting in localized or systemic infections, or be a consequence of mechanical ventilation, e.g., ventilator-associated pneumonia. In addition, some patients may have a prolonged intensive care unit (ICU) stay before developing brain death, and are therefore exposed to cross-contamination with organisms from infected patients in the ICU. This ICU exposure may result in overt infections, or an asymptomatic and undiagnosed carrier state.

Organs from deceased donors with severe infections, including bacteremia (2, 3), meningitis (4), and endocarditis (5), have been harvested and successfully transplanted with no evidence of adverse effects, i.e., no transmission of infections, no increase in rejection, and no influence on graft survival. Recently, however, there have been increasing reports of patients admitted to the ICU who are exposed to organisms resistant to most classes of antimicrobial agents, which may result in an asymptomatic carrier state or the development of a severe nosocomial infection, such as pneumonia or bacteremia. As potential organ donors are typically hospitalized in the ICU, it seems inevitable that they too will be exposed to these organisms.

We report a case of an undiagnosed infection with a multidrug-resistant (MDR) organism in a deceased organ donor, and report recipient outcomes.

Case description

Donor

A 36-year-old man with no significant medical background was admitted to the hospital after near-drowning. He underwent cardiopulmonary resuscitation at the scene and arrived in the emergency room in deep coma (GCS 3); papillary reflexes as well as spontaneous breaths were present at that time. He was transferred to the general ICU, where mechanical ventilation was continued. On the 5th hospital day, clinical examination was compatible with brain death and a trans-cranial Doppler demonstrated absent cerebral blood flow. Throughout the ICU course, the patient was noted to be hemodynamically stable with no evidence of active sepsis (normal white cell count, normothermia, no requirement for vasopressor support), and a chest x-ray was reported as being normal. Brain death was formally determined on the 6th ICU day and consent was obtained from the family for organ donation. At the time of organ recovery, a routine bronchoscopy was performed and bronchoalveolar lavage fluid sent to the laboratory for culture. Both lungs, both kidneys, and the liver were recovered and subsequently transplanted into 5 recipients. Two days after organ procurement sputum and bronchoalveolar lavage cultures obtained from the donor were reported as positive for carbapenem-resistant *Klebsiella pneumonia*e (CR-KP). Antibiotic sensitivity was limited to gentamicin, colistin, and tigecycline.

Recipients

Patient demographics and outcomes, both infectious and transplant-related, are shown in Table 1.

Liver

The liver recipient experienced mild graft rejection 2 months post transplantation; after receiving appropriate therapy, the patient made a full recovery, and liver function at 6 months was normal. No infectious complications were noted in the postoperative period. The patient did not receive any peri- or postoperative antibiotic treatment.

Kidneys

Regarding the 2 kidney recipients, no post-transplant infectious complications were noted, and graft function was normal in both patients 6 months post transplantation. Both patients received preoperative antibiotic treatment with intravenous (IV) cefazolin, according to local protocol. Neither patient received postoperative antibiotic treatment.

Lungs

Neither lung recipient was hospitalized in the immediate preoperative period. Both lung transplant procedures were performed in the same hospital as the donor; however, the recipients were admitted to the cardiothoracic ICU after transplantation. Both recipients received perioperative antibiotic prophylaxis with piperacillin-tazobactam, according to local protocol. Following the report of the positive donor sputum culture, both patients received IV colistin for 5 days.

One of the lung recipients was diagnosed with pneumonia 2 weeks after transplantation; *Proteus mirabilis* was cultured from repeated sputum cultures. The patient was treated with IV colistin and ciprofloxacin, and made a full recovery. Lung function was normal 6 months after transplantation.

The second lung recipient was a 50-year-old male patient, who had undergone a double lung transplant 8 years earlier because of cystic fibrosis. Because the patient had not been hospitalized for the 6 months pre transplantation, routine screening for CR-KP at admission was not performed. The present lung transplant operation was uneventful, and the patient was extubated the next day. Owing to paralysis of the left diaphragm, the patient required intermittent non-invasive ventilation.

Nineteen days after transplantation, the patient developed tachypnea and dyspnea, and a new infiltrate was apparent in the transplanted lung on a chest radiograph. Based on the results of the donor sputum, initial empiric antibiotic therapy with piperacillin-tazobactam was changed to colistin and tigecycline; however, his condition continued to deteriorate. In addition, dehiscence of the operation wound was noted and the patient underwent a surgical repair. A tracheostomy was performed at this time and his condition stabilized.

However, 1 week later (3 weeks after transplantation), the patient was noted to be hypotensive and oliguric, with a decreased level of consciousness. Blood cultures were positive for CR-KP in 5 different

Recipient demographics and outcomes

Recipient no/Age (years)	Organ transplanted	Postoperative infections	Acute rejection	Patient survival at 6 months	Graft function at 6 months
1/60	Liver	No	Mild, at 2 months	Alive	Normal
2/21	Kidney	No	No	Alive	Normal
3/17	Kidney	No	No	Alive	Normal
4/64	Single lung	Pneumonia, *Proteus mirabilis*	No	Alive	Normal
5/50	Single lung	CR-KP pneumonia at 4 weeks post transplant	No	Died 4 weeks post transplantation	

CR-KP, carbapenem-resistant *Klebsiella pneumoniae*.

Table 1

samples, despite the fact that he was receiving treatment with colistin and tigecycline, and the antibiotic sensitivity profile was the same as that of the pathogen isolated from the donor's sputum. Treatment with vasopressors and hemofiltration failed to improve the patient's condition, and he subsequently died 4 weeks after transplantation.

Discussion

The isolation of MDR organisms has been increasingly reported in critically ill patients in the ICU (6–8). Increased use of cephalosporins in the 1990s was accompanied by the emergence of Enterobacteriaceae possessing extended-spectrum β-lactamases. Carbapenems are recommended as first-line therapy for severe infections caused by these pathogens. However, as a result of wide use of these agents, carbapenem resistance increasingly has been reported. This resistance has been attributed to the combination of high-level production of AmpC β-lactamase, loss of outer membrane proteins, and recently to Class A KPC-type lactamases, which efficiently hydrolyze penicillins, cephalosporins, and aztreonam, in addition to carbapenems (8–10).

Klebsiella pneumoniae accounts for the majority of carbapenem-resistant Enterobacteriaceae. These isolates are particularly problematic because, on the one hand, they are frequently resistant to almost all classes of antimicrobial agents, with very restricted treatment options, and on the other hand, they are frequent nosocomial pathogens, commonly causing pneumonia and bacteremia in the ICU (11). In addition, patients with unrecognized colonization with carbapenemase-producing Enterobacteriaceae have been shown to transmit these bacteria in the hospital setting (12). Thus, patients in the ICU may become asymptomatic carriers of the organism, which may potentially result in flare-up of the disease at a later stage.

We have described our experience with a multiorgan deceased donor, an asymptomatic carrier of CR-KP in the respiratory tract, a condition that was not suspected before organ harvesting and transplantation. The post-transplant course for 4 of the 5 recipients, including those for liver, both kidneys, and one of the lungs, was largely uneventful. In particular, despite the fact that they did not receive specific antibiotic therapy post transplantation, none of these patients developed infections with the donor organism in the immediate post-transplantation period, and in addition, no adverse effects on transplant outcome were noted during the 6-month follow-up period.

Both lung transplant recipients received prophylactic colistin. One of the lung recipients developed a pneumonia from which *P. mirabilis* was isolated. The patient was treated with appropriate antibiotics, made an uneventful recovery, and was subsequently discharged from hospital. The other lung transplant patient, who had undergone previous lung transplantation, developed pneumonia in the transplanted lung 4 weeks after transplantation. Despite the administration of appropriate antibiotic therapy, based on the susceptibility of the organism cultured from the donor, a combination of colistin and tigecycline, the patient rapidly developed severe sepsis with multiorgan failure and subsequently died. Both sputum and blood cultures were positive for CR-KP phenotypically identical to the donor's isolates.

No fingerprinting analysis was performed to ascertain whether this was the same genotype isolated in

the donor. However, given the identical phenotypical similarity between isolates from the donor and the recipient, together with the relatively early post-admission development of pneumonia and bacteremia caused by this pathogen, the possibility of transmission of the donor organism to the recipient appears very likely.

Previous experience has stressed the importance of detecting pathogenic organisms in the donor with sepsis and administering adequate therapy, both to the donor and recipient, according to antibiotic sensitivities (13–15). Our present experience stresses the importance of the detection of asymptomatic carriers of CR-KP, especially in airway secretions; in this setting, it seems prudent that lung transplantation not be performed. However, it appears that the transplantation of all other organs could be permitted. This is based on the fact that the agents most widely used in the setting of MDR organisms, namely colistin and gentamicin, have poor penetration into the lung, but good penetration into other organs from which CR-KP may be isolated, including the kidneys.

In conclusion, our initial experience suggests that, in well defined conditions, organs from donors who are CR-KP positive may be considered for transplantation. Close recipient follow-up is mandatory in order to validate this approach. Finally, strict implementation of infection control measures is crucial to prevent infection and contamination of patients hospitalized in the ICU in general, and potential donors in particular.

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