Renal Transplantation from an Unrelated Living Donor to a Malignant Hyperthermia–Susceptible Patient: A Case Report

Marli Kern, CRNA, MSNA

A 56-year-old patient with renal insufficiency secondary to Alport syndrome presented for kidney transplantation from an unrelated living donor. The recipient had a medical history that included 2 episodes of malignant hyperthermia: in 1989 and 1991. On both occasions she was treated with dantrolene. The patient had not undergone muscle biopsy testing but was considered malignant hyperthermia susceptible (MHS) based on clinical history. Both the kidney donor and the recipient underwent nontriggering general anesthetics using total intravenous anesthesia techniques without the use of prophylactic dantrolene. Using this technique, the MHS kidney recipient did not experience a malignant hyperthermia episode perioperatively. The donor and the recipient had uneventful clinical courses, and to date the renal transplantation has been successful.

Keywords: Alport syndrome, malignant hyperthermia, nontriggering anesthetic technique, renal transplantation, total intravenous anesthetic.

Approximately 97,000 living donor kidney transplants have been performed nationwide since 1988; however, as of June 10, 2011, a total of 94,896 patients remain on the waiting list for kidney transplantation (Figure).1,2 Transplantation is the optimal treatment for patients with end-stage renal disease; therefore, the incidence of living donor transplantation is increasing. Living donor transplantation presents a unique set of anesthetic considerations.

The case presented here was further complicated by the fact that the recipient was malignant hyperthermia susceptible (MHS). Malignant hyperthermia (MH) is a rare genetic disorder of skeletal muscle triggered in susceptible humans by inhalation agents and/or depolarizing neuromuscular blockers (Table). This disorder results in a potentially catastrophic sequence of events, including hypermetabolism, skeletal muscle damage, increased sympathetic activity, and hyperthermia.3 The acidosis, hyperkalemia, rhabdomyolysis, and myoglobinuria associated with MH are particularly devastating to the patient with end-stage renal disease. Perhaps more importantly, such clinical sequelae would be undesirable in a newly transplanted kidney. There are at least 2 case reports of malignant hyperthermia during renal transplantation.4,5 Management of MH is more complicated in patients with end-stage renal disease because of preexisting and often severe electrolyte and acid-base abnormalities.5 To our knowledge, there are no previously published case reports of unrelated living donor kidney transplantation in MHS patients.

Case Summary
A 56-year-old, 60-kg woman known to be MHS present-
tation was scheduled on a Monday morning such that each patient was the first case of the day and week in her respective operating room.

The anesthesia machine in the donor’s operating room was prepared by changing the circuit and carbon dioxide absorber and flushing the system with high oxygen flows for approximately 1 hour. The donor was premedicated with midazolam, 5 mg, given in divided doses. General anesthesia was induced with fentanyl at 150 μg, 100 mg of lidocaine, and propofol at 150 mg. At this time, a remifen-

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**Table.** Malignant Hyperthermia: Triggering and Nontriggering Agents
Abbreviations: MH, malignant hyperthermia; NSAIDs, nonsteroidal anti-inflammatory drugs.

<table>
<thead>
<tr>
<th>Drugs likely to trigger MH</th>
<th>Drugs that do not trigger MH</th>
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<tbody>
<tr>
<td><strong>Potent inhalation anesthetics</strong></td>
<td>Nitrous oxide</td>
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<tr>
<td>Halothane</td>
<td>Narcotics</td>
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<tr>
<td>Isoflurane</td>
<td>Benzodiazepines</td>
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<td>Enflurane</td>
<td>Barbiturates</td>
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<td>Desflurane</td>
<td>Propofol</td>
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<td>Sevoflurane</td>
<td>Ketamine</td>
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<tr>
<td>Ether</td>
<td>Nondepolarizing neuromuscular blockers</td>
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<tr>
<td><strong>Depolarizing neuromuscular blockers</strong></td>
<td>Anticholinesterases and anticholinergics</td>
</tr>
<tr>
<td>Succinylcholine</td>
<td>Local anesthetics (amides and esters)</td>
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<tr>
<td></td>
<td>NSAIDs</td>
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<td></td>
<td>Calcium</td>
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**Figure.** Waiting List and Transplant Activity for Kidneys, 2000-2009
Abbreviations: SRTR, US Scientific Registry of Transplant Recipients; OPTN, US Organ Procurement and Transplantation Network. (Reprinted with permission from USTransplant.org.)
tantal infusion was started at 0.3 μg/kg/min, and a propofol infusion was initiated at 100 μg/kg/min. Endotracheal intubation was facilitated with vecuronium, 7 mg. (At the time of this transplantation, there was a shortage of cisatracurium, and our institution did not have cisatracurium or atracurium available for use.) Cefazolin (1,000 mg) was administered following induction, according to the surgeon’s request. General anesthesia was maintained with oxygen and air, continuous infusions of propofol (75 to 100 μg/kg/min), and remifentanil (0.2 to 0.3 μg/kg/min). Boluses of midazolam, fentanyl, hydromorphone, and vecuronium were administered as needed.

Meanwhile, the recipient’s anesthesia team prepared the anesthesia machine by changing the circuit and carbon dioxide absorber and flushing the system with high oxygen flows for approximately 1 hour. In addition, the vaporizers were removed from the anesthesia machine, and succinylcholine was removed from the anesthesia workstation. The malignant hyperthermia cart was immediately available just outside the operating suite. Anesthesia care partners and additional anesthesia providers were readily available.

The recipient was transported to the operating room. Premedication included midazolam, 2 mg, and diphenhydramine, 50 mg. Standard induction monitors were applied as well as a skin temperature probe in order to obtain a baseline temperature prior to induction of anesthesia. General anesthesia was induced with 150 μg of fentanyl, 120 μg of propofol, and 10 μg of etomidate. At this time, a propofol infusion was initiated at 100 μg/kg/min. Endotracheal intubation was facilitated with vecuronium, 6 mg. Methylprednisolone (1,000 mg), vancomycin (1,000 mg), and levofloxacin (500 mg) were then administered according to the surgeon’s request. Subsequently, an esophageal stethoscope with a temperature probe and an orogastric tube were inserted. A triple-lumen central line was inserted into the right internal jugular vein. The patient was monitored with electrocardiography, central venous pressure, pulse oximetry, capnography, noninvasive peripheral blood pressure cuff, nerve stimulator, bispectral index monitoring, and measurement of core temperature and urine output. Anesthesia was maintained with oxygen and air, a continuous infusion of propofol (60 to 100 μg/kg/min) and boluses of midazolam, fentanyl, hydromorphone, and vecuronium as needed.

Throughout the case the recipient’s temperature ranged from 35.1°C to 37.0°C, end-tidal carbon dioxide (ETCO₂) ranged from 28 to 45 mm Hg, and heart rate ranged from 65/min to 105/min. The patient was hemodynamically stable and showed no evidence of hypermetabolism. Based on the patient’s clinical picture at the conclusion of the case, the suspicion for an MH recurrence was extremely low. The surgical and anesthetic course had proceeded uneventfully, the patient was extubated, and transported directly to the intensive care unit (ICU). The ICU staff was alerted to monitor specifically for signs of MH, and dantrolene was available at the bedside.

**Discussion**

Alport syndrome is an inherited disorder of the genes encoding type IV collagen.7 Type IV collagen is the primary structural component of all basement membranes, including that of the glomeruli. Patients with this syndrome have hearing loss, ocular lesions, and progressive nephropathy.7 The risk of female patients with Alport syndrome progressing to end-stage renal disease is less than that for male patients. It is possible that our patient’s underlying disease was complicated by 2 previous anesthetic-induced episodes of malignant hyperthermia. Renal sequelae associated with MH may have exacerbated existing glomerular injury, perhaps hastening the patient’s kidney failure. In this case, the patient was to receive kidney transplantation from an unrelated living donor. Transplant candidates with Alport syndrome present a challenge in terms of living donation from a relative. Selection criteria for such a donation must take into consideration the fact that the patient’s family members may also have inherited this genetic defect and donor nephrectomy should be avoided if renal dysfunction is suspected to develop.8

Although Alport syndrome led to this patient’s need for transplantation, her history of MH was the primary concern during the perioperative period. The goal of anesthetic management in the MHS patient is to avoid an MH episode. Evidence-based medicine does not support pretreatment with dantrolene in MHS patients undergoing a nontriggering anesthetic.6 For this reason, we elected not to pretreat the MHS kidney recipient with dantrolene and to conduct nontriggering anesthetics using total intravenous techniques in both the donor and the recipient. The immediate availability of dantrolene as well as other MH supplies was, however, confirmed prior to commencement of the cases. In addition, the recipient’s anesthetic was designed to be as stress-free as possible. This permitted us to more readily associate clinical signs such as tachycardia with impending MH rather than with the stress of anesthetic induction or surgery.

The quantity of anesthetic gas needed to trigger an MH episode in a susceptible individual is unknown. For this reason, the goal of anesthetic care for MHS patients is to avoid triggering agents entirely, including volatile anesthetic gases. Cold ischemia time in living donor transplantation is very short in comparison to that of cadaveric transplantation. It is not inconceivable that a living donor organ exposed to triggering agents and then transplanted into an MHS patient could lead to an MH episode. Not only would this jeopardize the recipient, but it could ultimately lead to loss of an organ that was available only because a healthy, unrelated individual...
was willing to incur the anesthetic and surgical risks in order to donate it. Initiation of an MH episode in these circumstances because of a failure of the anesthesiology team to take all precautions necessary would be unforgivable, but could have easily occurred had the team not acted with such forethought.

We took precautions not only in the preoperative and intraoperative periods but also postoperatively. Because our patient would have been arriving to the Postanesthesia Care Unit (PACU) during a high occupancy time, the decision was made to bypass the PACU and take the patient directly to the ICU. It was our opinion that the potential for exposure to trace amounts of inhalational agents in the PACU should be avoided. There is little information in the literature regarding the level of anesthetic gas waste in the PACU environment. A pilot study conducted at The Johns Hopkins Hospital, Baltimore, Maryland, in the main PACU failed to detect levels of halogenated agents above the exposure level of 2 ppm recommended by the National Institute for Occupational Safety and Health (NIOSH). Byhahn et al did, however, report substantial concentrations of volatile anesthetics in the ambient air in the PACU based on infrared spectrometry. Furthermore, they showed that contamination of the ambient air in the PACU peaks when the unit is completely occupied.

Although the initial presentation of MH generally occurs intraoperatively, there are reports of postoperative onset of MH. Litman et al reviewed records of suspected cases of postoperative MH in the North American Malignant Hyperthermia Registry and found the latency period (time between the discontinuation of an anesthetic triggering agent and onset of MH) to be short: 0 to 40 minutes. None of these patients presented with hyperthermia without additional signs of MH. Accordingly, the ICU staff was alerted to assess for signs of hypermetabolism (including hypercapnia, tachycardia, and tachypnea), generalized rigidity, and signs of rhabdomyolysis such as brownish-colored urine.

This case report provides an example of kidney transplantation from an unrelated living donor to an MHS recipient with Alport syndrome. Given the discrepancy between organs available for transplantation and organs needed for patients on transplant waiting lists, living donor transplantation has become more prevalent. It is our hope that presentation of this case demonstrates a method of anesthetic management that makes living donor organ transplantation in recipients with MHS possible. Caution must be used when administering anesthesia in patients who are MHS. Although substantial progress has been made in the understanding of the disease, a great deal remains unknown. Even when conducting a trigger-free anesthetic, providers must be vigilant to detect and treat an MH episode.

REFERENCES


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