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Anesthetic Management for Resection of Hepatic Paraganglioma Metastatic From the Donor Organ in an Orthotopic Liver Transplant Recipient: A Case Report

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ABSTRACT

This is a case report of the anesthetic management for the hepatic resection of a metastatic paraganglioma in a patient with a history of prior orthotopic liver transplantation. Of interest, the metastatic paraganglioma originated from the donor organ. The patient is an 80-year-old woman with multiple medical problems including a history of cryptogenic cirrhosis who underwent successful orthotopic liver transplantation 9 years prior. She later presented with signs and symptoms of catecholamine excess suggestive of a catecholamine-producing tumor (paraganglioma or pheochromocytoma). Elevated urine catecholamine levels and radiographic evidence of a paraganglioma in the transplanted liver metastatic from the donor organ confirmed the diagnosis. Radiofrequency ablation of the tumor and surgical resection was previously attempted without success. We describe the anesthetic management for the successful resection of the metastatic hepatic paraganglioma, which was complicated by profound intraoperative hypertension and hypotension that necessitated the use of multiple vasoactive infusions, extensive surgical blood loss requiring blood transfusion, and difficult glycemic control in an insulin-dependent diabetic patient. The postoperative course is also described. This unique case presented the anesthesia team with challenges specific to both surgery for hepatic resection as well as for catecholamine-secreting tumors. We are not aware of any reports of paragangliomas of either donor or recipient origin involving a transplanted liver, making this the first such report to the best of our knowledge.

THE PATIENT, an 80-year-old woman with a history of cryptogenic cirrhosis of the liver, underwent an orthotopic liver transplant (OLT) in 2002. She initially presented several months after her transplantation with signs and symptoms of catecholamine excess, including symptomatic hypertension, tachycardia, sweating, and palpitations. Subsequent workup revealed evidence of excess catecholamine levels consistent with a diagnosis of a suspected paraganglioma metastatic from the transplant donor. She was initially treated with multiple radiofrequency ablations to the affected liver segments with little success, as well as with attempted wedge resection of the cancer in 2009. At least one of the radiofrequency ablations had been canceled due to severe hypertension and tachycardia associated with tumor manipulation. A computed tomography imaging study from June 2011 demonstrated interval increase in tumor growth with a 13 × 9-cm mass in the left lobe of the liver. In July 2011, she was taken to the operating room for complete resection of the tumor; we report the anesthetic management for this case.

PREOPERATIVE COURSE

In addition to cryptogenic cirrhosis and subsequent OLT, her medical history was notable for severe and poorly controlled hypertension treated with multiple antihypertensive medications, insulin-dependent diabetes mellitus, gastroesophageal reflux disease, recent diagnosis of deep venous thrombosis in the left femoral and popliteal veins, and chronic renal insufficiency. She had no history of coronary

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artery disease or congestive heart failure. Her preoperative medications included labetolol, tacrolimus, mycophenolate, pantoprazole, lamivudine, valsartan, Lantus insulin, warfarin, and pioglitazone. She had previously been prescribed phenoxybenzamine as an outpatient but was unable to tolerate the drug due to side effects of nausea and postural headache.

Urinary 24-hour catecholamine levels tested several months prior to the surgery were significant for an elevated urine norepinephrine of 585 μg/24 hours (normal range 15–80 μg) and a total metanephrine level of 11,123 μg/24 hours (normal range 180–646 if normotensive, <1300 if hypertensive). Urine epinephrine and dopamine levels were within normal limits.

Electrocardiogram revealed normal sinus rhythm with heart rate (HR) of 97. Preoperative stress echocardiography revealed no reversiable ischemia, preserved ventricular function, and diastolic dysfunction. Baseline creatinine was 1.4, hematocrit 35.5, INR 1.1.

INTRAOPERATIVE COURSE

The patient's preoperative blood pressure was 166/94 with HR of 84. Weight was 74 kg, body mass index 27.3. An awake radial arterial catheter was attempted but was unsuccessful. A modified rapid sequence induction with cricoid pressure was performed with 200 mg propofol, 50 mg esmolol, 250 μg fentanyl, and 50 mg rocuronium. After securing the airway, a double lumen central venous catheter was placed in the right internal jugular vein. Attempts at insertion of a radial arterial line were unsuccessful; subsequently a femoral arterial line was inserted. During this entire period the patient was hemodynamically stable with blood pressures ranging from 120 to 140/60 to 80 with HR 60 to 70. Anesthesia was maintained with 1:1 air/oxygen mixture with end-tidal 1.6% to 1.9% sevoflurane. After surgical incision the patient was tachycardic and hypertensive, with HR to 140 and blood pressures above 200/100. This was initially temporized with intravenous boluses of nitroglycerin and esmolol, followed by titration of nitroprusside and esmolol infusions and metoprolol 5 mg to maintain the heart rates below 100 and blood pressures of 130 to 150/60 to 80. With increased surgical dissection there was significant blood loss; arterial blood gases were obtained systematically and packed red blood cell transfusions were administered to maintain hematocrits between 27% and 30%. Significant hyperglycemia with blood glucose levels over 250 mg/dL was treated initially with 15 U of intravenous regular insulin and subsequent infusion at 8 U/h.

Immediately following the complete paraganglioma resection, the systolic blood pressure rapidly decreased to 100. Nitroprusside infusion was weaned off, and several 100 μg phenylephrine boluses were administered to stabilize the blood pressure. Continuing the esmolol infusion to maintain the HR below 100, a phenylephrine infusion was titrated to maintain target systolic blood pressures between 120 and 140.

Following completion of the surgery, the patient was transported to the recovery room intubated and sedated on a propofol infusion at 50 μg/kg/min, esmolol at 40 μg/kg/min, and phenylephrine at 0.7 μg/kg/min. The insulin infusion was discontinued as blood glucose decreased to 146 mg/dL. Total blood loss was estimated at 1500 mL. Total fluids administered included 5 U packed red blood cells, 3 L plasmalyte, and 1000 mL 5% albumin. Urine output for the entire 4.5-hour procedure was 1000 mL. The pathology specimen was a 16.3 × 13.4 × 8.9-cm portion of resected liver; the tumor itself was 11.7 × 10.5 × 8.8 cm with foci of apparent necrosis involving 40% to 50% of the cut surface. The margins were negative; biopsy noted a paraganglioma consistent with metastasis of donor origin.

POSTOPERATIVE COURSE

Phenylephrine and esmolol infusions were weaned off within hours of arrival to the intensive care unit (ICU) and the patient was extubated on postoperative day (POD) 1. On POD 2 the patient developed an episode of new-onset rapid atrial fibrillation that resolved with metoprolol. Cardiology and endocrinology services were consulted to assist in the management of atrial fibrillation, hypertension, and diabetes. On POD 9 the patient was discharged from the ICU. For the remainder of the hospitalization, the patient remained hemodynamically stable with no further episodes of atrial fibrillation. On POD 14 the patient was discharged home.

DISCUSSION

Extra-adrenal pheochromocytomas, or paragangliomas, presenting as liver tumors have been described previously.[1] While generally metastatic from the para-aortic region, primary intrahepatic paragangliomas have been reported.[2–4] To our knowledge, this is the first reported case involving the anesthetic management of the resection of a hepatic paraganglioma metastatic from the donor organ in an OLT recipient. We are not aware of any reports of paragangliomas of either donor or recipient origin involving a transplanted liver.

It is generally recommended that patients undergoing resection of catecholamine-secreting tumors are medically optimized in the perioperative period. Alpha-blocking agents are usually prescribed.[4] Phenoxybenzamine, an irreversible alpha-blocker, is considered a first line drug for this purpose.[5,6] Our patient had previously been prescribed phenoxybenzamine but was unable to tolerate the drug due to adverse side effects. While a lack of adrenergic alpha blockade may have contributed to her intraoperative hypertension, postresection hypotension was successfully treated with a phenylephrine infusion. Phenylephrine may not have been as efficacious in a setting with irreversible alpha blockade. Additional prophylactic antihypertensive medications in the preoperative period were withheld due to the

potential for significant hypotension after tumor resection and the likely possibility for significant blood loss. Indeed, vasoactive infusions were needed to support normotension after tumor resection. The titratable agents esmolol and sodium nitroprusside were used to manage the hemodynamic instability associated with tumor manipulation and surgical incision rather than prophylactic administration of longer-acting, potentially irreversible drugs such as clonidine, magnesium sulfate, calcium channel blockers, or labetolol.

A neuraxial technique in addition to general anesthesia was considered for intraoperative anesthesia, postoperative analgesia, and to decrease the neuroendocrine stress response. However, given the potential for significant blood loss, massive transfusion, and associated coagulopathy, both the surgical and anesthesia teams opted to defer in this regard.

During the hepatic resection the intraoperative management was complicated by significant bleeding, which was exacerbated by the hypertension and tachycardia associated with tumor manipulation. Invasive arterial monitoring and serial blood gas analysis proved invaluable in assessing blood loss and in maintaining intravascular volume status. Pancreatic islet cell dysfunction and accelerated glycogenolysis leading to hyperglycemia has been described in patients with catecholamine-secreting tumors.[7] Our patient presented with poorly controlled diabetes and significant intraoperative hyperglycemia, which necessitated insulin infusion.

Perhaps the most fascinating aspect of this case was that the hepatic paraganglioma in the transplanted organ was of donor origin. The increasing number of patients requiring OLT and a relatively stable number of donor organs has resulted in a shortage of suitable grafts for recipients.[8,9] This has lead to an increase in the transplantation of extended criteria donor organs.[9,10] A contraindication to orthotopic donation includes all transmissible malignancies. Donor organs are typically screened for malignancy via serum liver function tests, abdominal ultrasound, and frozen section liver biopsy. We do not know whether the donor patient was symptomatic from the undiagnosed paraganglioma, whether the tumor was of metastatic or primary origin, or what the extent of the patient's disease process was at the time of donation.

The donor organ was no doubt screened and considered acceptable for transplantation, but a relatively rare malignancy was not noticed in the screening process and was transmitted to our patient. This case was an unusual presentation of a rare diagnosis that provided the anesthesiologist with many significant challenges.

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