studies demonstrating the optimal duration of antifungal therapy; however, in most case reports, the length of treatment has ranged from 2 to 12 months, depending on whether concomitant surgery was performed. Timing for surgery is not defined. In general, mortality is 65% with surgery and approaches 100% without surgery. The presence of lung or sinus disease by Cladophialophora in the absence of neurologic signs and/or symptoms warrants monthly neurologic assessment for at least 6 months. Brain imaging should follow the occurrence of neurologic signs or symptoms to look for cerebral phaeohyphomycosis. Antifungal therapy may be guided by susceptibility testing but should not be delayed while speciation is in progress. Duration of antifungal therapy must be individualized, radiologic resolution of cerebral lesions may be one helpful criterion. The feasibility of surgical intervention should be considered in all patients with cerebral phaeohyphomycosis. We suggest that early surgical intervention may be the most prudent course when dealing with infections in immune compromised hosts.

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REFERENCES


DOMINO HEPATIC TRANSPLANTATION USING THE LIVER FROM A PATIENT WITH PRIMARY HYPEROXALURIA

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Background. We report a case of domino liver transplantation using the liver harvested from a patient who underwent a combined liver and kidney transplantation for primary hyperoxaluria (PH).

Method. A cadaveric liver transplantation was performed in a 19-year-old man with PH. In a second step, the PH liver harvested from the first patient was transplanted in a 69-year-old man with hepatitis C-related cirrhosis, not a candidate for a classic liver graft owing to multifocal hepatocellular carcinoma.

Results. At 8 months after transplantation, the domino recipient has normal hepatic function and no signs of tumoral recurrence, but he progressively developed hyperoxalemia, hyperoxaluria, and renal insufficiency.

Conclusion. Regarding the favorable postoperative clinical evolution, domino liver transplantations using livers from PH patients may represent a new opportunity for marginal candidates for liver transplantation. However, the progressive renal insufficiency expected in such domino recipients should limit this procedure to selected cases.

The shortage of cadaveric organs for liver transplantation led to the development of new techniques to expand the donor pool. These include living related, split, and sequential or domino liver transplantation. In the domino procedure (1), the liver harvested from a patient undergoing a liver transplantation is used as a donor organ for a subsequent graft in a second liver recipient. Until now, this approach was described using the liver from patients transplanted for familial amyloid polyneuropathy (2). In these patients, the only liver dysfunction is the overproduction of transthyretin, leading to chronic amyloid deposition and slowly progressive polyneuropathy. Therefore, the use of these organs for domino transplantation was judged acceptable for aged recipients or in cases of advanced intrahepatic malignancies. Patients undergoing liver transplantation for primary hyperoxaluria (PH) represent another group that may contribute to domino liver grafts. PH is a rare genetic disorder caused by a deficiency of the liver-specific enzyme alanine: glyoxylate amino-
transf erase ( AGT ), resulting in liver oxalate overproduction, hyperoxaluria, widespread calcium oxalate deposition, nephrocalcinosis, and end-stage renal failure (3). In these patients, except for the specific enzymatic defect, the function and anatomy of the liver are normal. The evolution of the disease is variable, probably in relation to residual enzyme activity in some cases. Inasmuch as in humans AGT was found at any significant extent only in the liver (4), it is rational to propose these patients for enzyme replacement therapy by a liver transplantation. In case of secondary renal insufficiency, the optimal treatment for PH patients is a combined liver and kidney transplantation to correct both the liver oxalate overproduction and the renal failure (5, 6).

MATERIALS AND METHODS

A 19-year-old man with PH was selected as a candidate for a combined liver and kidney transplantation. He experienced the first episodes of urinary tract infections during the first year of life, and urinary calculi were demonstrated at the age of 7 years. The diagnosis of PH was made on the basis of hyperoxaluria and later confirmed by hepatic biopsy showing the complete absence of AGT catalytic activity. Renal function progressively worsened, and hemodialysis was required at the age of 18 years. Hepatic workup, including liver tests, liver biopsy, magnetic resonance imaging, and celiac arteriography, was normal, leading us to consider the potential use of this liver for a domino transplantation. The patient gave his informed consent for this procedure. Concomitantly, an ABO-identical 69-year-old man with hepatitis C-related Child A cirrhosis was evaluated for a liver transplantation. He previously had a resection of the left hepatic lobe for a hepatocellular carcinoma up to 2 cm at the age of 15, 5, and 2 mm that contraindicated a liver transplantation under classic conditions (7). As a comorbid factor, the patient presented a history of diabetes without evidence of renal insufficiency (pretransplant creatinine clearance was 95 ml/min; normal is 75 to 150 ml/min). The patient was informed of the possibility of realizing a domino transplantation using the liver from a patient with PH and gave his consent for the procedure. Particular attention was given to the risk of renal complications and the possible need for hemodialysis in the long term. When a compatible cadaveric donor became available for the PH patient, the operations were started in parallel in domino donor and domino recipient. The heptectomy in the domino donor was performed, leaving supra- and infrahepatic vena cava cuffs, followed by standard orthotopic liver transplantation and renal transplantation in the right iliac fossa. After flushing with University of Wisconsin solution on a back table, the domino graft was implanted in the second recipient in a piggyback fashion after 130 min of cold ischemia. The postoperative course was uneventful in the domino donor and the patient was discharged on day 30 with normal liver and renal tests. The domino recipient experienced a normal postoperative evolution and was discharged on day 25 with normal liver tests. A liver biopsy, performed 6 weeks after transplantation, showed no sign of acute rejection and confirmed the complete deficiency of AGT catalytic activity. In this patient, the prevention of renal oxalate deposits consists in maintenance of a urinary output in excess of 3 L/day, thiazide diuretics, sodium citrate, and avoidance of high-oxalate food. In addition, despite the absence of any enzymatic activity on biopsy, high-dose pyridoxine, a cofactor of AGT, was administered.

RESULTS

After transplantation, the domino recipient progressively developed hyperoxaluria and hyperoxalemia (Fig. 1). At 8 months, oxaluria and oxalemia reached the levels of 181 mg/day and 12.5 mg/L, respectively. This observation confirms, in this unique situation of a patient with a normal genetic background and acquired liver AGT deficiency, the absence of any extrahepatic enzymatic activity. In parallel, renal function worsened; creatinine clearance was 43 ml/min at 8 months, probably in relation with the hyperoxaluria but also with preexisting diabetes and cyclosporine nephrotoxicity (Fig. 1). Under hyperhydration and prevention of oxalate deposition in the urine, the patient did not present any episode of urinary stones until now. Eight months after transplantation, the α-fetoprotein serum level remains under the limit of detection, and no mass was seen on abdominal computed tomography scan or chest x-ray.

DISCUSSION

This case illustrates that domino hepatic transplantation using the liver from PH patients may offer an alternative for marginal recipients. Inasmuch as the AGT enzymatic activity is exclusively located in the liver, the hyperoxaluria will inevitably recur in the recipients of PH livers. The rapidity of the progression to oxalosis and renal insufficiency in such situations is unknown, but one could expect that nephrotoxic immunosuppressive drugs could play an additional detrimental role. However, the prevention of urinary stone formation by hyperhydration and thiazide diuretics may prolong the asymptomatic period in these patients. The evolution to renal failure clearly represents the limitation of this type of domino transplantation. In the present case this should be balanced with the natural evolution expected in a cirrhotic patient with a multifocal hepatocellular carcinoma.

Thus far, this type of domino transplantation could represent a therapeutic issue in marginal patients with advanced intrahepatic malignancies, either as a definitive graft in aged patients or, potentially, as a bridge to classic liver transplantation in younger patients.

FIGURE 1. Posttransplant evolution of oxaluria, oxalemia, and creatinemia in the recipient of the PH liver. Normal ranges for oxaluria and oxalemia are 10–40 mg/day and 1.0–2.4 mg/L, respectively.
RENAL CELL CARCINOMA DETECTED IN A CADAVERIC DONOR AFTER ORTHOTOPIC LIVER AND CONTRALATERAL RENAL TRANSPLANTATION IN TWO RECIPIENTS

FOUR-YEAR FOLLOW-UP

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Background. Although rare, renal cell carcinoma has been found during renal recovery for cadaveric organ transplantation. Previously, we reported this incidence to be 0.9%. In one cadaveric donor, the liver and left kidney had been transplanted before the discovery of renal cell carcinoma (T1) in the right kidney.

Methods. We retrospectively reviewed the medical records of two patients who had received cadaveric allografts from a donor with a known renal cell carcinoma.

Results. Both patients have been followed for 4 years with blood chemistries and chest x-ray every 3 months for year 1, every 4 months for years 2 and 3, and every 6 months thereafter. They also underwent allograft ultrasonad every 6 months and an annual CT scan of the abdomen. Both patients have shown no evidence of metastatic disease throughout their follow-up.

Discussion. In the rare instance that a patient receives an organ from a cadaveric donor with a known renal cell carcinoma, it is mandatory to follow these patients closely observing for both allograft recurrence and metastatic disease.

The transference of malignancy from cadaveric donor to transplant recipient is a rare but recognized complication of organ transplantation. This occurrence was first reported with the transference of malignancy in renal allografts (1, 2). Since these reports, patients with a known malignancy have been excluded from consideration as organ donors. Penn reviewed 270 transplant recipients who had received organs from donors with a known malignancy (3). Of these, 117 (43%) developed tumor recurrence.

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In a recent review at our center, we determined the incidence of renal cell carcinoma discovered at the time of cadaveric renal recovery to be 0.9% (5/553) (4). Fortunately, this occurrence is rare and the majority of malignancies are discovered before organ transplantation with all recovered organs being discarded. Several studies have documented the transplantation of organs from cadaveric donors who were subsequently found to have renal cell carcinoma after organ transplantation. Pliskin et al. (5) reported that a cadaveric renal allograft was transplanted before the discovery of a renal cell carcinoma in the contralateral kidney. The transplant recipient was fully counseled regarding the potential risks and elected to keep the kidney. The patient has undergone follow-up with serial CT scans and has been without evidence of malignancy. Sack et al. (6) reported on a cadaveric heart transplant recipient who received an organ from a patient who was subsequently found to have renal cell carcinoma. The transplantation procedure was in progress at the time of discovery of the renal tumor and too far along to be aborted. Postoperatively, the patient was followed for tumor development. Twelve months after transplantation, the patient was found to have metastatic renal cell carcinoma.

In July of 1996, organs were recovered from a 60-year-old black male deceased secondary to a cerebrovascular accident with associated intracranial hemorrhage. The donor’s abdominal organs were recovered and deemed appropriate for transplantation. The donor’s liver and left kidney were transplanted at Louisiana State University Health Science Center (Shreveport, LA). While the right kidney was being prepared for transplantation at a separate institution, a right renal mass was noted and biopsied. Pathology returned as renal cell carcinoma (1.0 x 0.6 cm, grade 1, T1). The donor had no evidence of nodal or metastatic disease.

The recipient of the cadaveric liver was a 50-year-old black female with polycystic liver and polycystic kidney disease (normal renal function). The patient had been