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Transplantation

BRIEF COMMUNICATIONS

ACCIDENTAL TRANSPLANTATION OF MALIGNANT TUMOR FROM A DONOR TO MULTIPLE RECIPIENTS[1]

Recently an ancient pathway in transplantation was accidentally retrod when a malignant tumor that was undiagnosed in the lifetime of a cadaveric multiple organ donor was transplanted to several recipients of various organs. The following is an account of the subsequent tragic events.

Case Report. A 36-year-old woman died of an apparent spontaneous cerebral hemorrhage. Her past medical history was significant only for multiple spontaneous abortions. Her liver, heart, and kidneys were transplanted into four different recipients in three different transplant centers.

The liver recipient. The liver was transplanted on April 25, 1986, into an 18-year-old woman whose native liver had been destroyed by non-A, non-B chronic active hepatitis. Her operation and postoperative course were unremarkable, and she was discharged 27 days later with normal liver function tests on cyclosporine 450 mg twice a day, prednisone 15 mg a day, hydralazine 50 mg four times a day, clonidine 0.1 mg twice a day, and furosemide 40 mg a day.

Seven weeks postoperatively on June 19, 1986, the patient began having nausea, vomiting, and abdominal pain, but no fever. She was readmitted to the hospital. Chest roentgenogram, blood analyses, lumbar puncture, and cholangiogram were normal. The graft vessels were patent by ultrasonography. The ultrasound detected an echogenic area in the right lobe of the liver not confirmed by computerized tomography.

Her symptoms continued, and a repeat chest roentgenogram obtained on July 8, 1986, showed a small infiltrate in the right middle lobe. Although the patient was still afebrile and the sputum culture showed normal flora, cefazolin was started empirically. On July 13, eleven weeks after transplantation, the patient began to complain of shortness of breath, dyspnea on exertion, and hypoxemia, with an arterial pO_2 of 47 mmHg. A diffuse interstitial and alveolar pulmonary infiltrate compatible with an opportunistic infection rapidly developed, but a specific diagnosis could not be established. The patient was placed on a ventilator. Repeat computerized tomography now showed an area of inhomogeneity in the posterior portion of the right lobe of the liver. She died on July 19, 1986, 85 days after transplantation.

The findings at autopsy included a technically perfect transplantation with no evidence of graft rejection. A malignant trophoblastic tumor (choriocarcinoma) was present in the right lobe of the liver and extensively throughout both lungs. There was no evidence of tumor in the ovaries or the uterus, and there were no products of conception in the uterus, fallopian tubes, or ovaries. Stored preoperative serum and postmortem serum from the recipient were then analyzed for beta human chorionic gonadotropin (B-HCG). Preoperatively, the results were negative, but 273,270 mIU/ml was found in the autopsy serum. An autopsy had not been done on the donor. However it was possible to study stored donor serum; the beta HCG level was 4880 mIU/ml.

Kidney and heart recipients. This information was reported to the procurement agency. On giving the information to the other participating institutions, it was learned that both kidney recipients had recently been readmitted for abdominal pain and fever. They underwent transplant nephrectomies, and both grafts were found to contain choriocarcinoma. One of the patients had disseminated disease and died a short time later. The other recipient had tumor confined to the kidney and is alive, without evidence of metastatic disease, on methotrexate chemotherapy five months after transplantation. The heart recipient is alive and well with no evidence of carcinoma after five months.

Conclusion. Dissemination of tumor and viruses by transplantation is a well-known and greatly feared problem. The transplantation of tumor from donor to renal recipient was shown to occur as early as 1964 (*1–4*). Because of the young age of most donors, silent malignancies are rare. When present in this youthful population, the tumor itself most commonly would be the cause of death—and therefore, under most circumstances, would eliminate the victim as a donor. In the case reported here the only clue to the malignancy was the retrospective connection between the multiple spontaneous abortions and the choriocarcinoma. No autopsy was performed, and no abnormalities consistent with choriocarcinoma were noted at the time of the multiple organ removal.

When expendable organs such as kidneys have been transplanted, stopping the immunosuppression and removing the organ have been reported sometimes to be curative (*2*), although not always (*4*). When organs are not expendable, chemotherapy may be an option. The discontinuation of all immunosuppression almost certainly would lead to rejection and to the need for retransplantation. If the malignancy were only in the transplanted organ, retransplantation could be curative.

As the results of transplantation continue to improve, so too will the demand for organs. It is hoped that the cadaveric organ pool will increase with this demand, so that only the most desirable donors will be used. However, it is inevitable that occasionally tumors or infectious agents will be transplanted with a lethal outcome. Rapid screening methods for tumor and viruses could limit this kind of problem. Donors should have a complete autopsy after completion of organ removal.

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REFERENCES

1. Martin DC, Rubini M, Rosen VJ. Cadaveric renal homotransplantation with inadvertent transplantation of carcinoma. JAMA 1965; 192: 82.
2. Wilson RE, Hager EB, Hampers CL, Corson JM, Merrill JP, Murray JE. Immunologic rejection of human cancer transplanted with a renal allograft. N Engl J Med 1968; 278: 479.
3. McIntosh DA, McPhaul JJ, Peterson EW, et al. Homotransplantation of a cadaver neoplasm and a renal homograft. JAMA 1965; 192: 141.
4. Starzl TE. Late results and complications. In: Starzl TE, ed. Experience in hepatic transplantation. Philadelphia: Saunders, 1969: 369.

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PANCREAS AUTOTRANSPLANTATION—UNSUITABILITY OF THE SWINE AS A MODEL

Autotransplantation of the pancreas in animal models is most helpful to test a variety of physiological or technical aspects of pancreas transplantation without the variable of immunological rejection. The lessons obtained from this methodology can then be applied in the experimental procedure of human pancreas allotransplantation. Animal models have thus been utilized to investigate the effect of a number of variables on the endocrine function of the graft. These variables include handling the exocrine secretions, replacement of the normal neurovascular supply, and the importance of portal vs. systemic drainage on the transplanted pancreatic hormone production.

In swine, many pancreatic allograft studies have been performed. The transplant experience with this animal has been acquired partly because the transplant immunology of swine has been characterized (*1*). Despite a lack of published reports of porcine autotransplantation experiments, we attempted to develop a swine autotransplantation model. There are several reasons for this effort. We have experience with almost a thousand swine in experimental models of hemorrhagic shock and pancreatitis and have developed reliable anesthesia and operative methods. In the modern era of animal rights issues, the swine is a less sensitive animal than the other large animal model—the dog. Anatomically the porcine pancreas is more similar to the human pancreas than that of the dog because the gland is a retroperitoneal organ and the pancreatic head wraps the portal vein, whereas in the dog the pancreas is mobile on a long mesentery and the pancreatic head does not envelope the portal vein. The firmness of the pancreatic parenchyma in swine is also similar to the gland in man. Therefore the technical aspects of pancreatic transplantation and pancreatic anastomosis, in our opinion, more closely resemble those in man. We therefore attempted pancreas autotransplantation in swine after reviewing favorable published descriptions (*2, 3*) of the vascular anatomy. We found the pancreatic arteries to be unsuitable for autotransplantation.

Female domestic swine weighing 25–35 kg underwent laparotomy through a midline incision during halothane endotracheal anesthesia. Sixteen animals underwent autotransplantation performed as described in man and dog (*4*). The pancreatic head and neck were excised, with a vascularized segment preserved in the form of the pancreatic body and tail supplied by branches of the splenic artery. The splenic vein provided venous drainage and was removed at the junction with the portal vein. Planned vascular anastomoses in the new heterotopic site were the graft's proximal splenic artery to the common iliac artery and the stump of the splenic vein to the common iliac vein. The pancreatic duct was left open to drain freely into the peritoneal cavity.

The blood supply to the pancreatic tail during these dissections was found to be extremely variable, and of 3 types (Fig. 1). In half the animals, pancreatic arteries to the pancreatic tail were derived from the proximal splenic artery near its origin. In the remainder, the blood supply to the pancreatic tail was either from the common hepatic artery or from the celiac axis. We were unsuccessful at preserving blood supply to any of the transplanted organ segments.

During autotransplantation in man and in the dog, the goal is to transplant the pancreatic tail and its pancreatic arterial supply. The latter usually is derived from the splenic artery. Once the vascularized segment has been successfully autotransplanted, the remainder of the pancreas (pancreatic head, neck, and body) in the dog is excised and not preserved. The endocrine function of the autotransplant is therefore easily assessed. The entire gland cannot be autotransplanted because the blood supply to both the pancreatic head and liver is derived from the common hepatic artery. This vessel cannot be interrupted without compromising hepatic blood flow resulting in liver failure. Therefore, whole vascularized organ transplants of pancreas can be accomplished only in the allotransplant model where the donor is sacrificed. In swine, pancreas transplantation has been totally of the allograft variety.

In our attempt at autotransplantation and preservation of the animal, the approach was to preserve the relocated pancreatic tail and then excise the remaining pancreatic parenchyma from the duodenum. This procedure is quite successful in the dog (*4*). Previous published reports on the vascular anatomy of the swine pancreas have indicated that there were definite pancreatic arteries arising from the splenic artery (*2, 3*). When pancreatic arteries were found arising from the splenic artery in our study, they were millimeters from the origin of the splenic artery. This area of the splenic artery is the site of reimplantation. The vascular anastomosis of the proximal splenic artery was technically difficult if not unfeasible. In the remaining dissections, the pancreatic arteries were