Section X

TRANSPLANTATION

Chapter 140

CRITICAL CARE IN KIDNEY TRANSPLANTATION

ANDREI STIEBER, MD
ROBERT D. GORDON, MD
J. WALLIS MARSH, Jr, MD
J. THOMAS ROSENTHAL, MD
THOMAS E. STARZL, MD, PhD

Almost 30 years have passed since the first serious attempts at cadaveric renal transplantation, which is now a common occurrence. By 1984, more than 60,000 renal transplants had been performed. Although the surgical technique is now standardized, methods of immunosuppression have continued to change from body irradiation in the beginning (1,2), to 6-mercaptopurine (3), then azathioprine alone (4) or together with steroids (5), and finally cyclosporine (6) as a single agent (7) or in combination with steroids (8–11). Polyclonal and, recently, monoclonal antilymphocyte antibodies have been used to supplement conventional therapy for treatment of severe acute rejection (12–14).

Increased awareness within the medical profession and among the general public of the improved graft survival being obtained with current methods of immunosuppression has increased the number of patients with end-stage renal disease seeking transplantation. Although organ donation has also increased, supply continues to fall short of need. Furthermore, there is an ever-increasing pool of patients with high levels of preformed cytotoxic antibody for whom it is difficult to find a suitable organ donor. This, more than any other factor today, determines whether or not an organ transplant can be performed on an individual in a reasonable amount of time.

The technical aspects of kidney transplant surgery are such that the procedure can be safely performed by any well-trained surgeon. However, organ procurement surgery, particularly the ever more frequent multiple organ procurement, remains an area in which insufficient training, outdated technique, and inflexible personal habits can jeopardize the quality of renal allografts and, at the same time, the viability of other retrievable organs. Given the current demand for and success of extrarenal transplantations, every organ donor today must be considered for multiple organ donation and every transplant surgeon is obligated to become familiar with the requirements of successful multiple organ procurement. Similarly, nurses and physicians working in ICUs must be alert to the possibility of organ donation and skilled in the care of the multiple organ donor. Surgical techniques have been developed for early *in situ* cooling and en bloc removal of the kidneys with minimal dissection in the brain-dead cadaver donor. These methods allow the safe removal of extrarenal organs without compromising the quality of the renal allografts (15–17).

Today, very few renal transplant recipients require admission to the ICU. However, postoperative management of the renal transplant recipient continues to require special skill and judgment; serious complications, although infrequent, require intensive care. The transplant surgeon must continue as primary physician in the postoperative period, working in collaboration with specialists in critical care and nephrology. The training of the transplant surgeon includes all disciplines relating to the care of the immunosuppressed surgical patient such as immunology, infectious disease, electrolyte and acid-base physiology, respiratory care, nutritional support, and interpretation of diagnostic tests including biopsies, nuclear and CT scans, and ultrasonography.

This chapter will describe the current practices of the renal transplantation program at the University of Pittsburgh. This experience is almost entirely limited to cadaveric renal transplantations. In our opinion, direct crossmatch between donor cells and recipient serum in conjunction with cyclosporine-steroid therapy gives results good enough that the use of living related donors is justified only in special circumstances. Other centers, however, continue to use living related donors regularly because of the shortage of cadaver donors.

PRETRANSPLANT EVALUATION AND MANAGEMENT

Candidates for renal transplantation are first seen in an evaluation clinic, where a thorough history is obtained and a physical examination is performed. Laboratory and diagnostic tests, including liver function tests, hepatitis screen, blood type and HLA A, B, and DR tissue typing, panel reactive antibody, viral serology, ECG, chest and abdominal films, and voiding cystourethrogram are obtained. Psychiatric and social worker evaluations are also routinely performed, and potential candidates from other dialysis centers are evaluated by our nephrologists. Other specialty consultations are obtained as necessary. All diabetic patients receive a stress thallium test and a cardiology consultation. Coronary angiography is obtained only if need is suggested by the results of the stress thallium study and upon the recommendation of the cardiologist.

Once the evaluation phase is completed, each case is reviewed by a transplantation committee consisting of surgeons, nephrologists, social workers, and transplant nurse coordinators. Waiting time to receive an organ varies from a few months to several years, depending on the amount of preformed cytotoxic antibody, health status, and availability of allografts. Fresh serum samples are obtained each month for measurement of percent reactive antibodies (PRA) to a panel of lymphocytes from randomly selected individuals and for donor-specific crossmatching as organs become available. Patients with high levels of antibody or with a history of recent blood transfusion are crossmatched with a serum sample collected on the day of transplantation.

PREPARATION FOR OPERATION

On admission for transplantation, the patient is immediately weighed and given an oral dose of 17.5 mg/kg of cyclosporine. Routine blood counts and chemistries, a chest x-ray, and ECG are done, and specimens for viral cultures and titers are collected. Dialysis is performed if necessary, based on the judgment of the transplant surgeon and the nephrologist. The time lapsed since the last dialysis, the serum K^+, and evidence of fluid overload on physical examination or chest x-ray are important factors. Prompt allograft function is difficult to predict and should not be relied upon in making the decision whether or not to dialyze the recipient immediately prior to transplantation. If there is any doubt, it is better to perform preoperative dialysis, since dialysis within 24 hours after surgery will frequently result in bleeding in the surgical wound.

A cleansing enema is then given, since postoperative ileus can be considerably more threatening in the presence of a colon loaded with feces. Intravenous cefazoline is administered on call to the operating room. After the induction of anesthesia, a Foley catheter is placed into the bladder, which is then distended with 100 to 150 ml of 0.25% neomycin solution to sterilize the bladder and facilitate implantation of the ureter.

Use of heparin during the period when the iliac vessels are crossclamped for anastomosis to the kidney is at the discretion of the operating surgeon. Most of our surgeons do not use heparin routinely. Just prior to the completion of the vascular anastomoses and revascularization of the allograft, 1 gram of methylprednisolone is given intravenously; mannitol or furosemide is administered by the anesthesiologist, under the surgeon's guidance, depending on the central venous pressure (CVP) and venous turgor. The allograft is then placed in a suitable position and the transplant ureter is implanted into the recipient bladder. After a final inspection for complete hemostasis and proper position of the graft, the wound is closed. Drains are not routinely used.

IMMEDIATE POSTOPERATIVE MANAGEMENT

Fluid Management

After surgery, the patient remains in the anesthesia recovery unit until stable and alert, usually 2 to 3 hours. Urine output and CVP are measured every 2 hours for the first 24 hours, then once each nursing shift. Depending on the initial response of the graft and on the CVP readings (maintained between 10 and 15 cm H_2O), fluid boluses, diuretics, or both are given to support urine output and preserve urine flow. In patients with low serum albumin levels, salt-poor albumin or plasma protein fraction may be effective.

Fluid challenges must be done with restraint. Patients with oliguria can easily be overloaded and then require urgent dialysis. Early dialysis after transplantation may result in bleeding in the surgical wound; if dialysis is needed, it should be done with minimal anticoagulation.

Postoperative urine output is replaced with 5% dextrose in 1/2 normal saline (D51/2NS) according to the following protocol: (a) for output of >300 ml/h, replace 4/5 of the amount; (b) for output of 150 to 300 ml/h, replace total amount; or (c) for output of <150 ml/h, replace total amount plus 40 ml/h.

Immunosuppression

Steroids are begun at 200 mg/day in four divided doses and tapered according to the following schedule:

1. Methylprednisolone 50 mg IV q 6 h × 4, then
2. Prednisone 40 mg p.o. q 6 h × 4, then
3. Prednisone 30 mg p.o. q 6 h × 4, then
4. Prednisone 20 mg p.o. q 6 h × 4, then
5. Prednisone 20 mg p.o. q 12 h × 2, then
6. Prednisone 20 mg p.o. qd.

After 8 hours, unless the patient has an obvious ileus, fluids are started orally and the diet advanced as tolerated. Cyclosporine is started at 17.5 mg/kg p.o. daily given in two divided doses. If oral fluids and medication are not tolerated, an equivalent dose of IV methylprednisolone is substituted for prednisone, and cyclosporine is given intravenously 4 to 6 mg/kg·day in two divided doses.

The Foley catheter and the CVP line are discontinued on the second day unless circumstances require otherwise. Complete blood count, electrolytes, blood urea nitrogen, creatinine, and cyclosporine trough levels are obtained daily, and the cyclosporine dose adjusted accordingly. Baseline nuclear renal flowgram and sonogram are obtained on the first postoperative day and are repeated weekly in patients with significant graft dysfunction.

EARLY POSTOPERATIVE COMPLICATIONS AND THEIR MANAGEMENT

Rejection

Diagnosis

The direct crossmatch obtained prior to transplantation prevents most cases of hyperacute antibody-mediated allograft rejection. In patients with high titers of preformed cytotoxic antibodies, accelerated rejection may still occur, occasionally with a pattern of disseminated intravascular coagulation (18). Accelerated acute rejection is often severe and difficult to treat. Close monitoring of coagulation is necessary and renal scans are obtained daily to check for the presence of blood flow to the allograft. Infarcted allografts must be promptly removed.

Most patients will experience some degree of acute cellular rejection during the first 3 weeks after transplantation. This will be heralded by any combination of symptoms and laboratory findings including malaise, fever, arthralgia, allograft swelling and tenderness, decreased urinary output, leucocytosis, and elevation of BUN and creatinine. Renal flow scans and sonograms usually show diminished flow and function (19). Ultrasound should show no evidence of outflow tract obstruction, and may show graft swelling and prominence of the renal pyramids.

In doubtful cases, a percutaneous needle biopsy can be performed. There is a significant risk of hemorrhage and arteriovenous fistula in the graft associated with conventional needle biopsy; therefore, we do not routinely biopsy renal allografts. Fine-needle aspiration techniques recently advocated by Hayry et al. (20–22) may be preferable and safer.

The surgeon must be extremely alert during this delicate early post-transplantation phase. Cyclosporine absorption is highly variable, and careful monitoring is required to prevent blood levels from falling dangerously

low. Intravenous cyclosporine should be added to the therapy if oral absorption of the drug is unsatisfactory, as often happens in diabetics. Obese patients may also require intravenous supplementation until fat stores are saturated and satisfactory blood levels of cyclosporine can be maintained by oral administration alone.

Treatment

Mild cellular rejection will usually be reversed with a single intravenous bolus of steroids (1 gram of methylprednisolone in adults and 1 gram of hydrocortisone in children). Moderate rejection, or rejection that responds only partially to bolus therapy, can be treated with a repeat of the initial postoperative taper of high-dose steroid. Severe, steroid-resistant rejection or accelerated acute cellular rejection is best treated with a 10- to 14-day course of OKT3 monoclonal antilymphocyte antibody (OKT3 Orthoclone[R], Ortho Pharmaceuticals, Raritan, NJ).

OKT3 has several advantages over conventional polyclonal antilymphocyte globulin (ALG) including ease of administration, higher efficacy, and fewer side-effects. Anaphylaxis or anaphylactoid reactions are uncommon. Most side-effects occur only with the first few doses, and can often be prevented by premedication with antihistamine and low-dose steroids. Our results with this therapy have been extremely gratifying (13,14) and there have been no fatal side-effects in our experience with this drug. Failure of an allograft from acute cellular rejection is unusual with OKT3 therapy except in patients with a history of severe rejection of a previous allograft.

OKT3 is administered as an intravenous bolus by a physician over 5 minutes at a dose of 5 ml (5 mg) for patients weighing over 35 kg, and 2.5 ml (2.5 mg) in patients weighing less than 35 kg. Pulmonary edema was observed in overhydrated patients given OKT3 during early trials of the drug; therefore, a chest x-ray is recommended within 24 hours before the start of therapy. The patient is premedicated with 1 gram of intravenous hydrocortisone 30 minutes prior to receiving the first dose of OKT3, and with 250 mg of hydrocortisone 30 minutes prior to receiving the second dose of OKT3. Other premedications given each day are 25 to 50 mg of diphenhydramine p.o. or IV and 650 mg of acetaminophen p.o. or p.r. 30 minutes prior to OKT3. Epinephrine, oxygen, and hydrocortisone should be available.

Vital signs must be measured frequently for 4 hours after the first two injections and for 2 hours after subsequent doses. OKT3 is a murine globulin; a major limitation of OKT3, as with polyvalent globulins, is that it can be given for only one course in most cases, since these patients form antimurine antibodies. "Rebound" rejection at the end of the course occurs in less than 20% of treated patients if cyclosporine therapy is at an adequate dose before the completion of antibody therapy.

Rejection occurring after OKT3 has been given may be treated with steroid therapy or by adding small amounts of azathioprine to the daily regimen, in the range of 0.5 to 0.75 mg/kg·day. However, in our experience at least 30% of the patients do not form antimurine antibodies, and may receive OKT3 for a second or even a third time (unpublished data). It is important, however, not to jeopardize the patient's life by excessive zeal in the treatment of persistent rejection.

Acute Tubular Necrosis

Acute tubular necrosis (ATN) occurs with a certain frequency in renal transplants; its frequency is mostly related to the length of cold ischemia (duration of storage) and the length of the warm ischemia period, if there has been any, during harvesting (21–23). Other factors contributing to ATN to a variable degree are lengthy preliminary dissection in the donor, episodes of blood pressure instability and/or ischemia in the donor, and the presence and length of warm ischemia during transplantation, particularly in old kidneys.

Diagnosis

The first thing to be done in the presence of anuria or oliguria after renal transplantation is to establish if the CVP is adequate, i.e., 5 to 6 cm H_2O or greater. If it is low—and it generally drops considerably after revascularization of the allograft, especially if the patient was dialyzed just prior to the operation—one or two boluses of intravenous fluids should be administered over a short period of time, followed by intravenous furosemide. If no result is obtained with these maneuvers, the intravenous fluid administration rate must be drastically reduced to 30 ml/h or less, lest the patient develop acute pulmonary edema requiring emergency dialysis with its danger of bleeding in the wound. Immediate diagnostic tests must be undertaken in order to rule out mechanical problems or accelerated rejection. Characteristically, the renal flow scan will show good flow, but poor function and the ultrasound with Doppler capability will demonstrate good vascular flow in both renal artery and vein, as well as absence of large fluid collections, or hydroureter. The renal flow scan will also be able to diagnose a disruption of the ureteroneocystostomy by demonstrating extravasation of the isotope during the delayed function phase of the study.

Management

Once the diagnosis of ATN has been established, the extremely cautious management of fluid intake and frequent monitoring of serum electrolytes are of paramount importance. As previously mentioned, pulmonary edema is a real threat, as is hyperkalemia. If either of the two occurs, intensive care and emergency dialysis may become necessary. ATN is a reversible phenomenon in most cases and usually resolves within 2 to 3 weeks, although it may last several months. Some centers treat the patients with steroids, azathioprine, or antithymocyte globulin or monoclonal antibody preparations for 1 week to 10 days, or until the resolution of the problem, adding cyclosporine to the regimen only when the ATN has resolved. At our center, we maintain the cyclosporine doses unchanged, since most ATN cases resolve anyway (although possibly over a slightly longer period of time) and cyclosporine's immunosuppressive properties are advantageous.

Infection

Infection remains a constant threat in the immunosuppressed patient. The danger is particularly acute during the early postoperative period of high-dose steroid and cyclosporine therapy. Infection is the most common cause of patient mortality after renal transplantation, and is

often caused by surgical errors and/or excessive immunosuppression. The highest index of suspicion and aggressive treatment are required to prevent and combat sepsis. Fever or other symptoms of infection should be immediately investigated and can never be dismissed as trivial.

Bacterial

Bacterial infections present either as localized (wound, perinephric, intrarenal, urinary infection), or originating from distant systems (lungs, meninges, intra-abdominal, etc.). Either may present with bacteremia and septic shock. The organisms are often Gram-negative rods, usually resistant to many of the common antibacterial agents, or esoteric organisms rarely found except in immunosuppressed patients. *Streptococcus faecalis, Pseudomonas aeruginosa, Herellea, Serratia, Morganella morgagni, Listeria monocytogenes,* and *Legionella pneumophila* are the most common infective agents. If infection is suspected, multiple cultures are obtained and polyantimicrobial therapy is instituted without delay, even before the culture results become available. Patients in shock belong in the ICU, where careful monitoring can be accomplished and intubation performed at the first signs of impending respiratory failure. If the source of infection is not known, urine, sputum, blood and spinal fluid cultures, sonography, CT scan, and an indium-labeled WBC scan may all be necessary. Fluid collections detected by sonography or CT scan must be drained immediately, surgically or percutaneously, with drains left in place.

It is rare today to remove the native kidneys prior to renal transplantation. The possibility of abscesses developing in the native kidneys should not be overlooked. The CT scan is an extremely valuable tool in their detection. Advice from the infectious disease consultants can be very valuable, particularly in detecting sensitivity to new drugs or unusual combinations of antibiotics.

Pneumocystis carinii and *Legionella pneumophila* pneumonias are uncommon in most surgical patients, but are among the most frequent causes of pneumonia in the immunosuppressed patient. Dyspnea and hypoxemia may precede significant changes in the chest x-ray. Bronchoscopy with bronchoalveolar lavage (BAL) should be performed as soon as possible in order to confirm the diagnosis. Therapy with intravenous trimethoprim-sulfamethoxazole (Bactrim) and erythromycin should be started as soon as pneumonia is suspected without waiting for the results of diagnostic studies. Therapy can later be modified once the offending organism has been identified. Delay in treating *Pneumocystis* or *Legionella* pneumonia can be lethal. Even in the presence of a negative diagnostic study, if the clinical course is typical of *Pneumocystis carinii* pneumonia or Legionnaire's disease, therapy should be continued.

Therapy with Bactrim frequently results in the elevation of serum creatinine levels, which is reversible when the drug is reduced or withdrawn. Bactrim toxicity can be distinguished from cyclosporine toxicity and rejection by appropriate monitoring of cyclosporine blood levels and the usual diagnostic tests for rejection (nuclear flow scan, ultrasound, and occasionally biopsy).

Patients with *Pneumocystis carinii* pneumonia often need ventilatory support. The clinical findings often seem similar to acute respiratory distress syndrome (ARDS). It is therefore tempting to improve oxygenation by increasing positive end-expiratory pressure (PEEP) and keeping the concentration of inspired oxygen relatively low, while hydrating the patient to maintain adequate venous return. We believe that high oxygen concentration for a few days, in conjunction with relatively low PEEP and conservative use of fluids, is more effective and safer, since the potential oxygen toxicity is balanced by the benefits of improved cardiac performance and avoidance of pneumothorax and pneumomediastinum from pulmonary "blow-out."

We recommend prophylactic therapy with trimethoprim-sulfamethoxazole for all patients for 6 months after transplantation. One single-strength tablet taken at bedtime affords significant protection from *Pneumocystis* pneumonia and usually does not significantly raise serum creatinine. Patients who are allergic to sulfa drugs can be given trimethoprim alone.

Fungal

Fungal infections, although uncommon, also occur with higher frequency than in nonimmunosuppressed patients. *Nocardia asteroides* or *Cryptococcus neoformans* can cause pneumonitis or meningitis that may remain quite indolent for long periods of time, leading to progressive deterioration of the patient and possible death. *Candida* infection may complicate wound hematomas or rupture of the kidney, and may also cause disabling GI infection such as severe esophagitis. Mycostatin oral suspension ("swish and swallow") is given four times daily for 3 to 6 months after transplantation to reduce the risk of oral and esophageal candidiasis. Amphotericin B and 5-fluorocytosine are given intravenously for major systemic monilial infections.

Viral

In our experience, bacterial infections are better tolerated and usually easier to treat in patients treated with cyclosporine and low-dose steroids than in patients treated with conventional azathioprine and high-dose steroid therapy. However, viral infections remain a common and dangerous problem, even with cyclosporine therapy. The agents most frequently involved are cytomegalovirus (CMV), herpes virus (HV), and Epstein-Barr virus (EBV).

Localized herpes lesions can be treated with topical and oral acyclovir, but more extensive mucocutaneous lesions and generalized herpes require treatment with intravenous acyclovir. Patients with normal renal function are given 10 mg/kg every 8 hours. The dose should be adjusted to the current level of renal function.

Systemic infection with CMV may present with malaise, fever, possibly cough and shortness of breath, elevation of liver enzymes, leucopenia, and atypical lymphocytes on peripheral blood smear. EBV has been associated with the development of pseudolymphomatous lesions, as discussed below.

Treatment of all major infections should include reduction or even cessation of immunosuppression, particularly steroids, without which therapy will be ineffective or incomplete. For the renal transplant recipient, graft loss can be managed by returning the patient to dialysis. Uncontrolled sepsis means death.

Vascular Complications

Arterial

Arterial complications (thrombosis and disruption) are almost invariably technical in nature. The only notable

exception is that of arterial thrombosis in accelerated rejection, in which intrarenal arteriolar thrombosis leads to increased vascular resistance, diminished flow, and subsequent occlusion of the larger vessels.

Acute oliguria or anuria following an initial postoperative period of good graft function must be considered as an indication that an acute vascular accident, either arterial or venous, has occurred. The patient may complain of acute pain over the graft; graft tenderness and hematuria are common findings. With arterial thrombosis, the graft may not be swollen. The patient should be taken to the operating room promptly for exploration. Occasionally, an arterial vascular accident can be salvaged, but usually allograft nephrectomy is required.

Disruption of the arterial anastomosis is quite rare. It is heralded by sudden onset of excruciating pain in the area of the allograft, swelling, cessation of urine output, and signs of hypovolemic shock. The disruption of the anastomosis may behave like a dissecting aneurysm, with periods of tamponade and stabilization in between rebleeding and enlargements until the final, catastrophic rupture. In these patients, the first episode of acute pain may be erroneously attributed to acute rejection and treated with steroid boluses (24,25). A sonogram is often diagnostic and a renal flow scan may demonstrate extravasation during the perfusion phase. Disruption of the vascular anastomosis is a life-threatening event requiring emergency exploration, allograft nephrectomy, and, if feasible, repair of the iliac artery. If the iliac artery cannot be repaired, it can often be ligated without the necessity for grafting. In the exceptional case in which grafting is required, we have used arterial homografts when available (26). Synthetic prosthetic materials are contraindicated for local *in situ* repair, since the wound is often invaded by *Candida* species. Serial sonograms are used to monitor for the development of pseudoaneurysms. In the unusual case in which extra-anatomical bypass of the iliac artery has to be undertaken, it can usually be deferred to a later operation and synthetic materials can be used.

Venous

Venous thrombosis is a relatively rare complication, and it is usually due to kinking of an improperly positioned allograft, excessive stretch on a short vein, or other technical fault in reconstruction of the renal vein. Thrombosis of the allograft renal vein presents with severe pain, swelling, diminished urinary output, and gross hematuria. Allograft nephrectomy is always necessary.

The left renal vein is usually of sufficient length so that it is easy to implant. If the vena cava has been left attached to the right renal vein, it can be used to add length, or free grafts of donor iliac vein can be used. Less attractive but sometimes necessary alternative reconstructions involve anastomosis to the proximal end of a divided internal iliac or, in cases of extreme difficulty, external iliac vein. In rare instances, thrombosis of the renal vein may occur in conjunction with an occlusion of the entire femoro-iliac axis in the recipient. We have not seen the latter, despite the fact that we do not employ systemic heparinization during the crossclamping phase.

Rupture of Allograft

Rupture of the transplanted kidney can occur during episodes of acute rejection in which there is sudden and severe swelling of the organ. Since the introduction of cyclosporine, such severe acute rejection episodes have become rarer. They occur predominantly on the convex border, in a plane between lobar arteries, probably an area of decreased resistance. Rupture presents with the sudden onset of pain and swelling of the allograft, as well as signs of occult bleeding. A renal flowgram may show extravasation of contrast material during the perfusion phase, but it may be difficult to distinguish extravasation from allograft rupture and vascular anastomotic dehiscence. Immediate surgical exploration is indicated. Small fractures may be repairable with absorbable sutures and/or hemostatic materials, while larger ruptures require nephrectomy, usually total (27). Chronically ruptured kidneys surrounded by clot are invariably colonized by fungi.

Urological Complications

Ureteral Ischemia

Urological complications are always the result of technical errors, occurring during either harvesting (and "back table" work) or recipient operation. Sloughing of the donor ureter is secondary to disruption of the blood supply to the ureter, which receives all its flow from the donor renal artery. In most instances, severance of a low polar artery is the culprit, but "stripping" of the ureter during preparation of the allograft may accomplish the same thing. Dissection between the kidney and ureter that is carried proximally to the horizontal line passing the lower pole of the kidney should immediately raise suspicion of injury to the ureteral blood supply. After revascularization, the ureter should be carefully observed for color changes and venous turgor, and, at the time of trimming for the ureteroneocystostomy, cutting across without hemostasis will show if the bleeding is brisk enough. If there is any doubt as to the viability of the distal ureter, a ureteroureterostomy or ureteropyeloneostomy using the recipient's ipsilateral ureter should be done. In this event, the ipsilateral native kidney should be removed.

Ureteral necrosis after transplantation usually presents with hydroureter and urinary leak. Leg and testicular (or labial) swelling and drainage of fluid from the wound are signs of a possible urinary leak. Ultrasound and flow scans help determine the diagnosis. Percutaneous nephrostomy or internal stenting can be used to control drainage; some injuries will heal if well drained (28–30). In addition, such measures can aid in definitive repair. Ureteroureterostomy of proximal donor ureter or ureteropyeloneostomy to distal recipient ureter over an internal stent can be done to salvage the graft, combined with ipsilateral native nephrectomy. The ureteral stent is then removed cystoscopically after 6 weeks.

Ureteral Stenosis and Obstruction

Stenosis may occur at the ureteroneocystostomy due to incorrect suturing, crushing of the delicate ureteral tissue with sutures or forceps, or by strangulation inside the submucosal tunnel. It also may occur at higher levels in the ureter, secondary to compression by the testicular cord structures in males or the round ligament in females, or by the inferior epigastric vessels, if not tied and divided. Surgical intervention is usually necessary in order to correct these problems, although percutaneous nephrostomy also has been useful (29,30).

Lymphocele

Ligation of the tissue covering the recipient's iliac vessels during skeletonization is the safest way to prevent lymphoceles. Diathermy may be sufficient, but it is not as reliable. Ureteral obstruction by a lymphocele usually presents during the first 3 months after transplantation with increased BUN and creatinine, decreased urine volume, and a mass effect. Sonography shows hydronephrosis and fluid collection. Marsupialization of the lymphocele via "peritoneal window" performed through an intraperitoneal approach allows drainage of the lymphocele into the free peritoneal cavity to relieve the extrinsic compression of the ureter. It is tempting to treat obstructing lesions by percutaneous needle drainage, but the lesions almost always recur quickly and may become infected. Percutaneous sampling may be useful for diagnostic purposes to rule out other lesions such as an abscess or urinoma.

Ileus

Ileus is almost always present in the immediate postoperative period as a result of the retroperitoneal dissection. It usually resolves rapidly, but it sometimes requires repeated enemas and cathartics, as well as nasogastric decompression. It is more frequent and troublesome in diabetic patients and after long operations. It is important to prepare patients for renal transplantation with a large-volume enema in order to have a relatively empty colon during and after surgery.

Massive colonic dilatation (Ogilvie's syndrome) is a serious complication that may result in bowel wall necrosis and spillage, and may require hemicolectomy. Aggressive use of enemas and decompression colonoscopy is indicated. If these measures fail, decompression colostomy is required. If bowel perforation occurs, colectomy, ileostomy, broad-spectrum antibiotics, and reduction or withdrawal of immunosuppression are indicated.

Hypertension

Hypertension is common in patients with end-stage renal disease, and is aggravated by cyclosporine and the high-dose steroids taken after transplantation. Hypertension is the most frequent indication for admission to the ICU early after surgery and may be severe enough to result in cerebrovascular accidents, pulmonary edema, heart failure, or myocardial infarction. Treatment requires continuous arterial pressure monitoring in the ICU. Intravenous labetalol (given intermittently in doses of 20 mg first, then 40 mg every 10 to 15 minutes until blood pressure is controlled or a total of 300 mg has been reached, or as a continuous drip, 1 to 2 mg/min), hydralazine, or nitroglycerin can be be used to bring the blood pressure under control. Nitroprusside should usually be avoided because of the potential for cyanide toxicity in patients with renal failure. Fluid overload should be treated with vigorous diuresis, if possible, or dialysis.

Cyclosporine Toxicity

Cyclosporine toxicity may be difficult to differentiate clinically from rejection. Additional tests such as renal flow scans and needle biopsy may be necessary to establish a diagnosis. Severe toxicity can rapidly lead to renal failure with fluid overload, hyperkalemia, and renotubular acidosis. Patients with cyclosporine toxicity and fluid overload may experience seizures requiring treatment with dilantin or barbiturates. In severe cases, patients may require admission to the ICU for monitoring and respiratory support. Cyclosporine is drastically reduced or even stopped temporarily, and rejection is managed with alternative therapy with azathioprine or monoclonal antibody.

A different form of cyclosporine toxicity, which is uncommon and more prone to occur in elderly patients, presents with progressive confusion and even delirium. Cyclosporine must be withdrawn until the sensorium clears and can be reintroduced slowly once symptoms have subsided.

Pancreatitis

Pancreatitis after renal transplantation can be catastrophic and progress rapidly to multiorgan failure and death within a few days. More often the course is less rapid, but no less lethal, with only a gradual deterioration and progression to sepsis. If the patient survives, it is often possible for the allograft to be saved by reintroducing immunosuppression once the situation has stabilized. The patient should be treated in the ICU with appropriate cardiorespiratory monitoring and support; immunosuppression should be stopped. Allograft rejection is suggested by platelet and fibrinogen sequestration and graft swelling, and requires graft nephrectomy.

Fortunately, severe pancreatitis after kidney transplantation has been uncommon in our experience since the change from azathioprine-high dose prednisone to cyclosporine-low dose prednisone therapy. We have had only two cases, with one death.

LATE COMPLICATIONS THAT MAY REQUIRE INTENSIVE CARE

Infection

Although the incidence of infection decreases rapidly after 3 to 6 months post transplantation, life-threatening infections do occur and need special care. The most frequent and dangerous agents in late infections are *Pneumocystis carinii, Legionella pneumophila,* CMV, EBV, fungi, varicella-zoster virus, and tuberculosis. All these infections require severe reduction or cessation of immunosuppression, and admission to the ICU is often necessary. Specific agents, if available, usually must be used at or above the maximal dose (acyclovir, amphotericin B, 5-fluorocytosine, trimethoprim, zoster immune globulin, etc.).

Rejection

Acute rejection is quite unusual late after transplantation if immunosuppressive therapy has been maintained. Diarrhea and drugs, both of which may interfere with cyclosporine absorption, and patient noncompliance are the most frequent reasons for inadequate therapy. Intensive care is rarely required except for the complications of increased immunosuppression.

Lymphoproliferative Disorders

An increased incidence of post-transplant lymphoproliferative disorders (PTLDs) has been described with all forms of immunosuppression, but has been seen more frequently since the introduction of cyclosporine (31–33).

PTLDs usually occur during the first post-transplant year. The patients may present with fever, weight loss, and/or lymphadenopathy. High titers of antibody to EBV are found and positive EBV cultures can be obtained in many patients, especially those treated with cyclosporine. The disease may be mono- or polyclonal. Lymph node and tonsillary biopsy may be helpful, but tonsil biopsies may result in serious complications of which acute respiratory distress is the most life-threatening and requires intensive care, intubation, and respiratory support.

The treatment of choice is reduction of immunosuppression, which will usually lead to total remission of the disease (34). Occasionally, debulking of large lymphomatous masses such as infiltrating and obstructing lesions in the intestinal tract may be necessary. The temptation to treat with chemo- or radiation therapy while maintaining immunosuppression should be resisted.

Hypertension

The management of hypertension early after renal transplantation has been discussed above. Chronic rejection, recurrence of the primary renal disease, or noncompliance with medication may cause attacks of acute severe hypertension of an extreme degree. Rarely, late bilateral native nephrectomy is required for control. Allograft renal artery stenosis is now a less frequent cause of post-transplant hypertension, since today it is common to use end-to-side techniques of arterial anastomosis in which a Carrel patch of donor aorta is sewn to the side of recipient iliac artery. Stenotic lesions that occur distal to the renal artery origin may be successfully treated by balloon angioplasty. Lesions at the renal artery orifice are often less amenable to balloon dilatation because they often are the result of atherosclerotic disease in the wall of the native iliac artery.

CONCLUSION

For most patients experiencing renal transplantation today, recovery is rapid and relatively uneventful. A brief stay in the postanesthesia recovery unit is followed by a 7- to 14-day recuperation on the regular hospital floor. The trend in today's cost-conscious environment is for early discharge with close follow-up in the outpatient clinic. Although most patients will experience some allograft rejection, it is usually responsive to therapy with steroids or antilymphocyte antibody. Only a small percentage of patients experience side-effects or complications severe enough to warrant admission to the ICU. Acute fulminant rejection with allograft rupture, severe pancreatitis, and death from bacterial sepsis are now uncommon. Hypertension is the most frequent indication for invasive monitoring and intensive care. Viral and opportunistic infections remain a significant threat, but mortality from infection after renal transplantation is now less than 5%.

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