Renal Transplantation

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The first Renal Transplantation ever to be carried out in Malta was performed on the 22nd April, 1983, a day that may well be included in the Medical History of our Islands. This event is another step forward following the introduction, not very long ago, at St. Luke's Hospital, of Haemodialysis or as the layman would call it, the *'Kidney Machine'*.

What follows is not meant to be a case-presentation proper but is intended to serve as a base over which some pros and cons of renal transplantation, the subsequent management of the recipient and the possible complications that may commonly arise, could be forwarded to the reader in a hopefully simple and palatable manner.

Case:

A 45- year old, unmarried postman came to hospital in March '83 complaining of:

1. Intense Itching
2. Increasing pallor } since summer 1982
3. Increasing fatigue
4. Progressive breathlessness - worst in February 1983
5. Vomiting of eaten food

The patient has a history of albuminuria (at around the age of 20) following an upper respiratory tract infection. Since the age of 18 he has been a heavy smoker (approx. 50 cigarettes daily). About 18 months before his admission to hospital (March '83) the patient had a respiratory tract infection and his symptoms as listed above seem to have started then and continued since. There were no other significant findings in his Past History or in his Family History.

Following a medical examination and a battery of laboratory investigations, the patient was diagnosed as having ACUTE RENAL FAILURE.

The patient's health deteriorated rapidly and peritoneal dialysis was instituted. Improvement followed. Kidney transplantation was contemplated for this middle-aged bachelor and after the decision was finalised he was put on haemodialysis (towards the beginning of April '83). The surgeons concerned stated that the operation was feasible at St. Luke's Hospital itself.

Choice of Donor:

The donor in this case was the living sister of the patient. A close blood relative was chosen as the best possible donor since, as a survey published in April 1973 showed, the closer the relation between donor and recipient the higher the survival rate over an 8-year period was. The success rate for unrelated cadaver donors was considerably less, for the same 8-year period. Apart from this, cadaver donors in Malta present many other problems - availability as well as moral and ethical.

Two main criteria may have to be fulfilled if the tendencies for rejection of the allograft are to be minimised:

1. HL-A compatibility
2. Blood Group (ABO) compatibility

between donor and recipient.

The HL-A system is said to be a strong one and therefore thought to assume a major importance in considering transplantation of tissues. These antigens are widely distributed in tissues but are not present in red blood cells. The RBC's on the other hand, contain antigens of the ABO system (ABH antigens). Since leucocytes carry all the known HL-Antigens, leucocyte agglutination and cytotoxicity tests are carried out to detect the presence or absence of the antigens. A *cross-match* between donor lymphocytes and recipient serum is then performed to confirm the results of the above tests. Well matched transplants (HLA-wise) sometimes do poorly whilst poorly matched transplants can do well. Although most units continue to match, some no longer do and simply rely on the ABO compatibility.

When a live donor is chosen he must essentially be medically healthy: preferably no hypertension; no systemic disease; no renal disease; and donor must possess two well functioning kidneys. The donor must therefore be adequately screened. Preferably the kidney to be transplanted must by supplied by not more than two arteries, hence a flush renal arteriogram and a selective renal angiogram are carried out on donor preoperatively. An ultrasound investigation or an intravenous pyelography are also done.

The patient himself must be thoroughly assessed medically: a Barium meal may be necessary to exclude peptic ulceration which, if present, could be aggravated by steroid therapy post-operatively. A chest X-Ray is necessary to exclude chest infection particularly tuberculosis; intractable urinary tract infection is an indication for bilateral nephrectomy.

Surgical Technique:

The left kidney from the donor is opted for since it has longer blood vessels leading to and from it. This kidney is rotated and placed extraperitoneally in the patient's right hemipelvis. The renal artery is anastomosed usually end-to-end to the internal iliac artery or if a cadaveric kidney is used the renal artery together with a patch of aorta is anastomosed end-to-side to the internal iliac artery. The renal vein is sutured end-to-side to the external or common iliac vein. The ureter is implanted in the bladder through a submucosal tunnel. Alternatively, the recipient's ureter may be anastomosed to the renal pelvis of the donor kidney.

If a right kidney (from a cadaver usually) is to be implanted, it is rotated and put in the recipient's left hemipelvis.

Management:

1. Suppression of Immunological Reaction which causes Graft Rejection:
   - AZATHIOPRINE 2-3 mg/kg body weight It is started before operation and continued post-operatively. The doses are decreased as renal function resumes.
   - ANTILYMPHOCYTIC SERUM (purified to IgG) can be a potent immunosuppressive but is still in the experimental stage.
2. Steroids
   - PREDNISOLONE 2 mg/kg started on the day of operation. Doses are decreased over 3 months gradually to a maintenance dose of 15 mg daily.
3. Fluid Balance
   - Hourly measurements of urinary output. The same volume is replaced with Dextrose Saline up to a urinary output of 200 ml/hr.
   - Insensible loss is replaced by 20 ml Normal Saline/hr.

Complications:

(A) Of Renal Transplantation itself:

1. Acute Tubular Necrosis
2. Rejection (a) Hyperacute (b) Acute (c) Chronic
3. Stricture or Fistula at Ureteric Anastomosis
4. Renal Artery (or vein) Thrombosis or Stenosis.
5. Urinary Tract Infection
6. Tertiary Hyperparathyroidism

- Acute Tubular Necrosis
  - — usually seen in cadaveric kidney due to prolonged total ischaemia time.
  - — donor was hypotensive before death
- Hyperacute Rejection
  - — is seen in some cases during the operation itself.
  - — antibody dependent.
  - — occurs if prior exposure has led to sensitisation.
- Acute Rejection
  - — 5-7 days post-op. Usually happens in cycles, the periods between which progressively becomes longer.
  - — T-cell dependent
  - — Clinical features:

  Symptoms: Lassitude, patient feels unwell, anorexia, oliguria, anuria, haematuria.

  Signs: Fever, ↑Blood Pressure, Kidney is enlarged and tender, ↑weight, unilateral leg oedema (on side of transplant) and scrotal swelling.

  Investigations: Leucocytosis, ↑B.U.N and serum creatinine, ↓Na^+ excretion, Proteinuria (in recurrent renal disease), Ultrasound:- enlarged kidney with echolucent areas in substance of kidney. Arteriogram:- decreased vascularity; vessels irregular (these features are reversed by Prednisolone therapy). Biopsy:- perivascular lymphocytic infiltration; interstitial oedema.
- Chronic Rejection
  - — detectable by biopsy long before clinical deterioration.
- Stricture or fistula at ureteric anastomosis
  - — inadequate blood supply of donor ureter.
  - — poor healing due to uraemia and immunosuppression.
  - — leakage of urine may follow.
- Urinary Tract Infection
  - — susceptibility is increased by immunosuppression.
  - — catheterisation of ureter for splinting the ureterostomy.
  - — catheterisation of urethra to protect cystostomy.
  - — any microbe can be responsible; bacteria, viruses, protozoa, fungi.
  - — septicaemia is a constant threat.
- Tertiary Hyperparathyroidism
  - — hypercalcaemia due to hypertrophy of parathyroid glands during long period of antecedent chronic renal failure.
  - — may be due to adenoma of parathyroids in some cases.
- N.B. Hypertension
  - — post-transplant hypertension may accompany acute or chronic rejection or renal artery thrombosis or stenosis.
  - — occurs in 18-83% of patients.
  - — Hypertension due to other causes must be excluded e.g. essential hypertension, recipient's original renal disease if nephrectomy has not been performed.
  - — It is an important risk factor for myocardial infarction and cerebrovascular accidents as well as for Renal Failure.
  - — a bruit is not always detectable in renal artery stenosis.

— angiography is an essential investigation to detect renal artery stenosis, however this is invasive and requires the use of a nephrotoxic contrast medium.
— Doppler ultrasonography sound-spectrum analysis is being used as a non-invasive screening procedure. (For a more detailed account, the reader is asked to refer to reference No.8 below.)

(B) Of Immunosuppression

1. Steroids
   (a) Impaired wound healing
   (b) Increased susceptibility to infection & sepsis
   (c) GIT bleeding; Pancreatitis
   (d) Avascular bone necrosis; Osteoporosis
   (e) Cushing's Syndrome
   (f) Cataract
   (g) Diabetes
   (h) Psychosis
2. Azathioprine (antimetabolite)
   (a) Hepatotoxicity
   (b) Bone marrow suppression

N.B. Sepsis
— is still a major cause of death in patients who have received a renal transplant. The severity and frequency of infection have been reduced by less aggressive immunosuppression.
— There is a place for perioperative antibiotic coverage but long-term antibiotics should be avoided.

(C) Long-term Complications include:

1. Atherosclerosis
2. Malignancy e.g. Lymphomas (reticulum cell sarcoma) and sarcomas of brain and skin after Antilymphocytic globulin.
3. Cushing's Syndrome with hypertension and Diabetes mellitus.
4. Peptic Ulceration and its complications.

Treatment of Rejection:

1. Prednisolone and Azathioprine together with intermittent high dose prednisolone.
2. Antilymphocytic globulin
3. Drainage of thoracic duct to deplete patient of lymphocytes.
4. CYCLOSPORIN A a cyclic polypeptide that has been shown to be a powerful immunosuppressant. Some investigators have been able to use it alone in the management of renal transplant patients whilst others have found it to be more effective in combination with low dose steroids.

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