

## Case 123

# A renal transplant recipient with a gastrointestinal haemorrhage

A 23-year-old nulliparous female teaching assistant underwent a kidney transplant for glomerulonephritis. She had been waiting on haemodialysis for 3 years before she was called in for a transplant. She was told that the long wait was because she had previous blood transfusions, but couldn't understand why this was.

The kidney had come from a deceased donor, a 46-year-old lady who had suffered a subarachnoid haemorrhage and who died on a neurosurgical unit in another part of the country. Death was certified using brainstem criteria.

The recipient's principal immunosuppression was tacrolimus, azathioprine and prednisolone, and at the time of transplant she had received a course of basiliximab, a monoclonal antibody to the CD25 antigen. She made an uneventful recovery, being discharged 7 days later with a serum creatinine of 98  $\mu\text{mol/L}$ .

### Why can having a previous blood transfusion make it more difficult to get a suitable kidney?

Previous blood transfusions, transplants and pregnancies are associated with the production of antibodies against the foreign major histocompatibility antigens (human leucocyte antigens, HLAs) that are expressed on the donor cells, or on the foetal cells in the case of sensitisation due to pregnancy. If a patient receives a transplant with any HLA antigens against which the recipient has preformed HLA antibodies, the kidney will be subject to hyperacute rejection and destroyed within minutes or hours. In order to avoid this, a cross-match test is performed whereby serum from the recipient, (which will contain any preformed antibodies), is mixed with donor lymphocytes, (obtained from donor blood, spleen or lymph nodes removed at the time of donation, and expressing donor HLA). HLA-antibodies will bind, and, in the presence of rabbit complement, cell lysis occurs: if

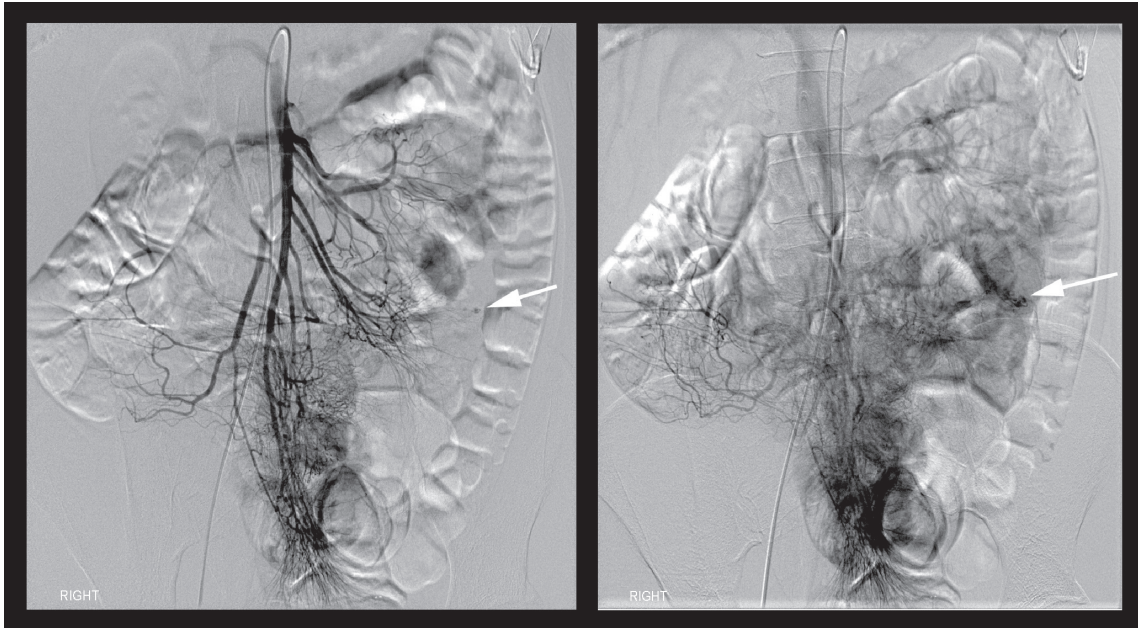
binding is observed, the cross-match test is deemed positive and the transplant cannot go ahead. Hence it can be seen that the presence of such antibodies makes it more difficult to find the patient a suitable matched kidney, avoiding any HLA antigens against which she has antibodies.

### What are the brainstem criteria used to diagnose death in the organ donor?

Death may be certified either by the absence of a heart beat or by the absence of brainstem function. To be diagnosed as dead by brainstem criteria the patient must be in a coma and maintained on a ventilator with a clearly identified cause of death. Hypothermia, intoxication, sedative drugs, neuromuscular blocking drugs and severe electrolyte and acid-base abnormalities must be excluded. If the above criteria are met, the following tests are performed:

- Pupil reflexes: Dilated and do not respond to direct or consensual light.
- Corneal reflex: Absent.
- Vestibulo-ocular reflex: Absent. When the head is turned passively the eyes remain fixed relative to the head.
- Vestibulo-caloric reflex: Absent. Slow injection of 20 ml of ice cold water into each external auditory meatus does not cause eye movement.
- Cranial nerve motor responses: Absent in the presence of adequate stimulation of a somatic area.
- Gag reflex: Absent, even to bronchial stimulation with a suction catheter.
- Respiratory movements: Absent, even when disconnected from a ventilator long enough for the  $\text{PCO}_2$  to rise above 6.65 kPa.

If the above criteria are satisfied the patient is declared dead. At that stage any prior wish to be an organ donor



**Figure 123.1** Selective superior mesenteric artery angiogram showing a bleeding point in the jejunum (arrowed).

is ascertained, as in this case, and organ donation can proceed following verification of death.

### What is a monoclonal antibody? Where else are they of surgical importance?

A monoclonal antibody is an antibody that targets a specific epitope on a cell surface, in contrast to polyclonal antibodies which target many epitopes. In transplantation the common targets for monoclonal antibodies are on T-lymphocytes, including the activated interleukin 2 receptor (the CD25 antigen, e.g. basiliximab).

In other fields of surgery they are important in the adjuvant treatment of malignancy (e.g. trastuzumab for breast cancer) and as anti-inflammatory treatment (e.g. infliximab, a tumour necrosis factor monoclonal antibody used for Crohn's disease). They have also revolutionized histopathological diagnosis (immunohistochemistry), identifying markers characteristic of certain diseases, such as CD117 in gastrointestinal stromal tumours.

### What are the common complications of immunosuppression?

Patients on immunosuppression are at risk of complications of the drugs themselves, and the complications of being immunosuppressed:

#### 1 Complications of immunosuppressive drugs:

- Tacrolimus and ciclosporin: Nephrotoxicity, neurotoxicity, diabetes mellitus.
- Mycophenolate: Diarrhoea, marrow suppression.
- Azathioprine: Marrow suppression, liver disease.

#### 2 Complications of being immunosuppressed:

- Infections, particularly infections by the herpes family viruses such as herpes simplex, varicella zoster and cytomegalovirus. In addition, opportunist infections with organisms such as *Pneumocystis jirovecii* (formerly called *Pneumocystis carinii*) and *Candida albicans*.
- Cancer, particularly skin cancers (possibly related to the papilloma virus) and lymphomas (related to the Epstein–Barr virus). In addition, most other cancers are more common.

*Six months after her transplant the patient presented with generalized lymphadenopathy. Biopsy of a groin node confirmed a lymphoma secondary to Epstein–Barr virus. She was treated with immunosuppressive reduction and a course of chemotherapy including the B-cell lytic CD20 monoclonal antibody rituximab. Two days later she experienced a brisk gastrointestinal (GI) bleed. Upper GI endoscopy and colonoscopy failed to identify the source of bleeding. She continued to bleed.*

### How would you investigate her next?

Most causes of GI bleeding will be picked up on endoscopy. If that is negative the bleeding point is somewhere between the second part of the duodenum and the ileocaecal valve. In the presence of active bleeding a mesenteric angiogram is the next investigation. In this woman, selective cannulation of the superior mesenteric artery suggested a bleeding point in the jejunum (arrowed on Fig. 123.1).

*The patient was taken to theatre where multiple necrotic areas of small bowel were found (Fig. 123.2) and resected. The specific point of bleeding was not identified but was presumed to be in association with one of these areas. The necrotic areas represented lymphomatous deposits in the small bowel that had been destroyed by the chemotherapy, in particular the monoclonal antibody therapy. Necrotic mesenteric lymph node masses were also noted. Following surgery she completed her chemotherapy and made a complete recovery.*



**Figure 123.2** Necrotic areas of small bowel.