humoral xenograft rejection and allowed kidney grafts to be life-supporting for as long as 83 days, does support contribution of xenothymus transplantation to graft survival and suggests a role for induction of T-cell xenotolerance.

Therefore, while recognizing that crucial advances have been achieved, we feel that translation of necessarily highly intense and prolonged immunosuppressive regimens to human xenograft recipients will be subject to significant risks of complications, and that induction of tolerance may be a safer option. As xenobody production may to large extent occur independently of T-cells, this would include tolerization of both B- and T-cells.

Nevertheless, we agree that other processes such as coagulation may play a pivotal role in xenograft rejection, and we look forward to learn from the first findings with the use of GalT+/- donor pigs transgenic for human anticoagulant genes.

Conflict of interest statement. None declared.

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doi:10.1093/ndt/gfl438

Letters

Advance Access publication 3 August 2006

Anti-neutrophil cytoplasmic antibody (ANCA)-associated microscopic polyangitis following a suppurative wound infection

Sir,

There is strong circumstantial evidence for the role of infections in the development of anti-neutrophil cytoplasmic antibody (ANCA) and ANCA-associated vasculitides. We describe here, a 74-year-old man who developed a wound infection after surgery for cancer and who was subsequently diagnosed with ANCA-associated microscopic polyangitis.

The patient presented with 2 months of frequent bowel actions, bright blood per rectum and weight loss. Physical examination including digital rectal examination was normal but colonoscopy demonstrated a mass in the sigmoid colon. Urinalysis and serum creatinine (0.093 mmol/l and 10.5 mg/dl, respectively) were normal. The patient underwent surgery and a 6.5 x 8 cm mass occupying two-thirds of the bowel circumference was removed by anterior resection. Histology confirmed an adenocarcinoma of the sigmoid colon with full thickness penetration of the wall, but had spread no further (Duke’s B).

One month after surgery, the patient began treatment with 5-fluorouracil. Within days of his second course, he developed pain in the abdominal wound and a purulent haemorrhagic discharge. A CT scan demonstrated a rectosigmoid abscess draining through the cutaneous fistula (Figure 1). A swab grew Escherichia coli, and the patient was treated with various antibiotics including ampicillin, gentamicin and metronidazole, as well as cefotaxime and ciprofloxacin. The amount of discharge lessened and the sinus closed over the following 6 weeks. The patient was not treated with further 5-fluorouracil.

Four months after surgery, the patient was readmitted with a painful knee, a temperature of 38.5°C and elevated C-reactive protein (123 mg/dl, normal <10). Abdominal CT scan showed no collection nor metastases. However, his creatinine had deteriorated to 0.223 mmol/l (25.1 mg/dl), urinary phase contrast microscopy demonstrated >500 000 glomerular RBC/ml (normal <12 000/ml), and he had a perinuclear ANCA 3+ with strongly positive myeloperoxidase (MPO)-ANCA. A renal biopsy demonstrated a pauci-immune segmental proliferative necrotizing glomerulonephritis and the patient was treated with high dose prednisolone and cyclophosphamide. Six months after starting this treatment he was admitted to the hospital with a small bowel infarction and subsequently died.

The close temporal relationship in this patient suggests the infection had a precipitating and probably pathogenetic role in the development of the ANCA-associated microscopic polyangitis. The association of infection, ANCA and vasculitis is well-recognized. Patients with Wegener’s granulomatosis and microscopic polyangitis often have preceding bacterial pulmonary infections [1,2], and those with nasal Staphylococcus aureus are more likely to relapse [3] unless they are treated [4]. In an experimental system, the immunization of rats with pasteurized sonicated proteins from E. coli and S. aureus resulted in circulating ANCA

Fig. 1. CT scan of abdomen shows the rectosigmoid abscess and track.
as well as a pauci-immune segmental necrotizing glomerulonephritis and mesenteric arteritis [5]. How infections produce ANCA is not clear but chronic suppurrative infections comprise mainly neutrophils, and the injection of rats with apoptotic (but not non-apoptotic) neutrophils generate ANCA [6]. Furthermore, infections themselves result in the surface expression of proteinase 3 and myeloperoxidase, and ANCA binds to these and activates the neutrophils resulting in a damaged vascular endothelium [7].

ANCA sometimes occur with malignancy or after antibiotics, but the temporal relationship in this patient is inconsistent with these as pathogenetic factors. The presence of arteriolitis in the initial renal biopsy, and the demonstration of an ischaemic bowel without atherosclerosis or embolism are more consistent with an overlap syndrome with polyarteritis nodosa rather than the diagnosis of microscopic polyangiitis alone.

Conflict of interest statement. None declared.

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doi:10.1093/ndt/gfl152

Advance Access publication 24 July 2006

Pathological rupture of spleen in a haemodialysis patient due to tuberculosis

Sir,

Atraumatic rupture of the spleen has been described as a condition with grave consequences, if unrecognized and untreated. The spleen can get ruptured in the following circumstances: due to trauma to a diseased spleen; trauma to a normal spleen; spontaneous rupture of a diseased spleen (pathological rupture) and spontaneous rupture of a normal spleen (spontaneous rupture) [1,2].

The true incidence of pathological rupture is unknown. A Medline search confirmed that 352 cases were reported between 1966 and 2000 [3]. The causes were wide-ranging, from infective, haematological, metabolic, drug-induced to iatrogenic.

Tuberculosis as a cause of pathological spleen rupture has been described in a few case reports [3]. No case report has been reported of a haemodialysis patient. We report a 27-year-old male patient with a diagnosis of hypertension, end-stage renal disease, on maintenance haemodialysis from August 2005, who developed sudden onset of pain in the abdomen, vomiting, and shock following a session of haemodialysis, in which heparin was also given. He had no prior complaints of fever, night sweats, chill, weight loss or anorexia. There was no other organomegaly or lymphadenopathy. A plain radiograph of the abdomen showed opacification of the left half, with relative paucity of bowel loops, due to fluid collection in the left half of the abdomen. A CT scan showed the presence of peri-splenic haematoma and blood collection in the abdominal cavity. The chest radiograph was normal. An emergency splenectomy was done along with a blood transfusion, as about 1.5 l of blood was evacuated from the abdominal cavity.

Oedema of the spleen may occur in uraemia [4]. The rupture appears to be precipitated by uraemic coagulopathy and the use of heparin, coupled with tuberculous infection. The tuberculous infection of the spleen has been reported in both immuno-competent and immuno-suppressed patients, albeit in the form of case reports [5]. It appears that there is no clear-cut way of diagnosing splenic tuberculosis other than a chance discovery on laparotomy and subsequent histopathological examination.

Conflict of interest statement. None declared.