Klatskin's tumour 10 years after successful cadaveric renal transplantation

I. H. Khan, N. M. Kernohan*, G. R. D. Catto and N. Edward

Renal Unit, *Department of Pathology, Aberdeen Royal Infirmary, Aberdeen, Scotland, UK

Case report

A 59-year-old Scottish male non-smoker, blood group O Rhesus negative, tissue type (A25, A31, B18, B27) received a cadaveric renal transplant in 1980. He had been on chronic hospital-based haemodialysis since 1973 for renal failure secondary to biopsy-proven chronic glomerulonephritis. The donor was a male aged 47 with blood group O Rhesus positive, tissue type (A2, Aw24, B15, B18). Maintenance immunosuppression was achieved with azathioprine 1.0 mg/kg body weight and prednisolone 0.2 mg/kg daily. A year following transplantation the patient had a partial focal seizure with residual right-sided weakness and was commenced on phenytoin 300 mg/day. His other medication included metoprolol 100 mg and allopurinol 100 mg/day. Between 1985 and 1990 he developed recurrent multifocal basal-cell carcinomata involving the scalp and skin over the chest, left shoulder and back, which were treated by excision on four occasions. In January 1992 he presented with right upper quadrant pain, pruritus and weight loss of 6 weeks duration. Liver function tests, which had hitherto been normal, revealed a raised serum alkaline phosphatase (647 U/l, normal < 105), a raised gammaglutamyl transaminase (1128 U/l, normal < 35) and a raised serum bilirubin concentration (59 μmol/l, normal < 22). Serum creatinine concentration was 120 μmol/l and haemoglobin 13.3 g/dl. He had never abused alcohol and had negative serology for cytomegalovirus, Epstein–Barr virus, and hepatitis A, B and C viruses. Ultrasound examination revealed dilated intrahepatic bile ducts and percutaneous transhepatic cholangiography revealed obstruction at the confluence of the right and left hepatic ducts suggestive of cholangiocarcinoma (Klatskin's tumour). The lesion was considered inoperable and a biliary stent was inserted percutaneously, resulting in resolution of his jaundice and pruritus. Six weeks later he was readmitted with recurrence of jaundice, pyrexia, and rigors, and despite antimicrobial and supportive therapy he died in hospital from septicaemia. Tumour histology on autopsy confirmed the diagnosis of cholangiocarcinoma involving the porta hepatis, and revealed several hepatic metastases (Figure 1).

Discussion

An increased incidence of neoplasia in patients on chronic immunosuppression is well recognized. Impaired immune surveillance, oncogenic viruses, and direct neoplastic action of immunosuppressive drugs have been suggested as possible mechanisms which increase the risk of cancers in transplanted patients [1]. For some tumours such as Kaposi’s sarcoma, the incidence may be as high as a thousandfold compared with the non-immunosuppressed general population [2,3]. Skin cancer, carcinoma of the cervix, and non-Hodgkin's lymphoma are frequently seen and a 6.9-fold increase in risk of developing renal-cell carcinoma has been reported [3]. The Australia and New Zealand...
Registry of renal allograft recipients [3] revealed that 50% of patients with renal transplants for more than 15 years developed neoplasia, the majority of which were skin cancers. Azathioprine immunosuppression in renal transplant recipients has been associated with a variety of hepatic disorders including acute liver necrosis, nodular regenerative hyperplasia [5], cholestasis, peliosis hepatis [6], and venoocclusive disease [7]. Azathioprine immunosuppression has also been associated with an increased incidence of cancers in non-transplanted patients and the Rheumatoid Arthritis Azathioprine Registry has reported 20 malignant conditions (predominantly lymphoproliferative disorders, myeloma, and lung cancer) in 530 patients treated with azathioprine over a period of 7 years [8].

In the general population malignant tumours of the bile duct are less common than those of hepatocytes, and aetiological factors of importance are clonorchiasis in the Far East, congenital anomalies of the biliary tree, and chronic ulcerative colitis. In bile-duct tumours involving the confluence of the right and left hepatic ducts, curative surgical resection is seldom possible, because of local invasion of hilar structures, and most patients require palliative biliary drainage for symptomatic relief [9]. The previously reported renal allograft recipient who developed cholangiocarcinoma also developed the tumour 10 years following cadaveric renal transplantation and, like the patient described here, had been on immunosuppression with prednisolone and azathioprine [4]. Other chemicals and drugs associated with cholangiocarcinoma include exposure to thorotrast, anabolic steroids, oral contraceptive agents, and methotrexate.

Changes in bile-duct morphology attributed to azathioprine have been described in renal allografted patients. Nine liver biopsies from six renal allograft recipients suffering from liver disease were examined. None of the patients had liver dysfunction prior to transplantation and all were negative for hepatitis B serology and were receiving azathioprine. Degeneration of bile ductal and ductular cells on light- and electron-microscopy were seen in all six patients. It is possible that several years of treatment with azathioprine may increase the risk of bile-duct tumours in renal transplant recipients.

References