Epstein-Barr-Virus-Associated Lymphoproliferation Arising in a Renal Allograft

E.R.		Maker
M.E.		Chappell
P.		Amlot
P.		Sweny
O.N.		Fernando
J.F.		Moorhead

Departments of Nephrology and Transplantation, Histopathology, and Immunology,
Royal Free Hospital, London, UK

Dr. E.R. Maher, Renal Transplant Unit, Royal Free Hospital, Pond Street, Hampstead, London NW3 2QG (UK)

Dear Sir,

After skin neoplasms lymphomas are the most common cause of malignancy in renal transplant patients. The risk of a transplant recipient developing malignant lymphoma is increased as much as 350 times [1]. Transplant-associated lymphomas frequently involve extranodal sites such as the brain or gastrointestinal tract, and a predilection to infiltrate the allograft has been noted [2]. Although involvement of the renal allograft as the initial presentation of lymphoproliferative disease has been reported [3,4], lymphoproliferative disease confined exclusively to the renal allograft has not been described. We report such a case occurring within 66 days of renal transplantation.

A 19-year-old male with end-stage renal failure from obstructive uropathy received a live-donor renal transplant from his mother. Donor-specific blood transfusions were not given preoperatively though 1 unit of blood was given preoperatively. The patient was immunosuppressed with prednisolone (15 mg/day) and ciclosporin. Trough levels of ciclosporin measured by a high-performance-liquid-chromatography method [5], ranged from 51 to 260 ng/ml (median 123 ng/ml) during the first 66 days posttransplantation. Primary graft function followed transplantation. Three courses of methylprednisolone (15 mg/kg for 3 days) were initiated on days 11, 16 and 30 for rejection episodes. The creatinine clearance improved to 41 ml/min. On day 66 he was readmitted because of a rise in plasma creatinine and the allograft was noted to be enlarged. A renal biopsy showed rejection but also contained foci of a dense infiltrate of large lymphoid cells with numerous mitoses not typical of rejection. Attempts at immunophenotyping these cells were unsuccessful on paraffin-embedded material. Plasma creatinine continued to rise despite antirejection therapy and a further renal biopsy was performed on day 76. A greater proportion of the biopsy contained the dense lymphoid infiltrate and immunophenotyping on fresh tissue showed it to consist of B cells which were CD19 + , CD21+ and HLA-DR+ but not expressing surface immunoglobulin or CD24, a marker of recirculating B cells. The B cells stained positively for Epstein-Barr-virus (EBV) nuclear antigen and HLA typing showed them to be of recipient origin. Insufficient material was available for gene rearrangement studies and demonstration of light chain restriction was precluded by lack of

expression of immunoglobulin. Whilst the histo-logical appearances and immunophenotype were consistent with a centroblastic lymphoma, there was no proof of monoclonality and EBV-associated lymphoproliferative disorders in transplant patients are often poly-clonal [6]. There was no evidence of lymphoproliferation elsewhere on clinical examination or on further investigation (chest radiograph, ultrasound and CT scans, gallium scan, liver function tests, biopsy of enlarged tonsil and bone marrow examination). Immunosuppression was withdrawn and haemodialysis commenced. Biopsies on day 84 and 92 showed progressive clearing of the B cell infiltrate which was replaced by T cells consistent with rejection. Transplant nephrectomy was performed on day 99. No residual B cell lymphoproliferative disease was detected. The patient had been seronegative and his mother seropositive for EBV before the transplant. Serial viral titres were consistent with a primary EBV infection acquired at or after transplantation. If the lymphoproliferation seen in the kidney was an example of a primary EBV infection, it was surprising that lymphadenopathy was not found elsewhere. The clinical course was reminiscent of the asymptomatic EBV seroconversion seen in

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children and was presumably modified by the immuno-suppression given. The patient is well on haemodialysis 6 months later.

The regression of this lymphoproliferative disease after cessation of immunosuppression is in accord with other reports [6]. EBV-associated lymphoproliferation has been implicated in the pathogenesis of transplant-associated lymphomas [7, 8]. Their predilection for the allograft may be related to it being a site of lymphocyte activation as activated B cells may be more susceptible to EBV-induced proliferation. In this case the renal allograft was not only the site of the lymphoproliferative disease but may also have been the mode of transmission of the associated EBV infection.

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Announcement

Sixth International Symposium of Nephrology

Montecatini Terme, Italy, June 1–3, 1989

This meeting continues the series of symposia which take place every 2 years in Montecatini Terme. The title of the Symposium is ‘Kidney, Proteins and Drugs’. Renal handling of proteins, pathophysiologic mechanisms of proteinuria, diagnostic applications and nephrotoxicity of drugs will be emphasized.

For information, registration and abstract

submission, contact: Claudio Bianchi, MD, Professor of Nephrology, Centra Nefrologico, Clinica Medica Generale 2, University of Pisa, I–56100 Pisa (Italy).

Erratum

In the article by Boyd/Lingwood

entitled ‘Verotoxin Receptor Glycolipid in Human Renal Tissue’

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the following error should be corrected: on page 208

last paragraph

the third sentence should read: ‘After washing

the plates were incubated overnight with purified VT [4] in 100 mMTris-saline buffer pH 7.4 at 4°C.’ and not ‘100 μ MTris-saline buffer’.