Case Report

Epstein–Barr-virus-associated post-transplant B-cell lymphoma presenting as allograft artery stenosis

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Introduction

Patients who have undergone renal transplantation are at considerable risk of lymphoproliferative disease, most commonly involving B lymphocytes, during the first year following transplantation. Although the exact incidence is not known precisely, the rate in these patients was reported to be 20 times higher than that in the general population [1]. There is strong evidence associating the Epstein-Barr virus (EBV) with the development of post-transplant lymphoproliferative disorders (PTLD). Extranodal involvement, often confined to the allograft, is a distinctive feature of PTLD. This report describes a case of EBV-associated B-cell lymphoma presenting as an extrinsic compression of the graft artery that produced an exacerbation of hypertension.

Case report

A 44-year-old woman with end-stage renal failure due to polycystic renal disease was placed on haemodialysis in May 1994 and underwent renal transplantation in November 1994 with a 1B, 1DR matched cadaveric kidney. The donor was a 43-year-old woman who had died of cardiac arrest 1 month after valve replacement. The recipient's pre-transplantation EBV serology showed IgG against viral capsid antigen (VCA), negative VCA IgM and no IgG against nuclear antigen (EBNA). The donor had IgG antibodies against both VCA and EBNA, but the assay for IgM antibodies was negative. Immunosuppression consisted of induction with ALG and methylprednisolone for the first 14 days. Cyclosporin was introduced on the 8th day and the maintenance immunosuppressive treatment was cyclosporin plus prednisone. Graft function was recovered after an initial period of oliguria. The post-transplant course was not complicated by rejection episodes. Viral serology on days 11, 18 and 25 demonstrated transient IgM antibodies to EBV VCA which disappeared on day 31 without any increase in IgG titre. Intravenous acyclovir (600 mg/day) was given from days 9 to 28. When the patient was discharged on day 31, her serum creatinine was 146 µmol/l and her systolic and diastolic blood pressures were kept at 130/80 mmHg with nicardipine and atenolol.

Seven weeks later she was readmitted with fever, cough, dyspnoea and hypoxaemia (PaO2 42 mmHg, PCO2 42 mmHg). Examination of bronchial washings disclosed Pneumocystis carinii. The patient was successfully treated with oxygen administered through a face mask, plus intravenous trimethoprim-sulphamethoxazole. The monthly ultrasound (US) and Doppler controls revealed some aliasing on colour mode and increased peak systolic velocities (2.5 m/s) on the mid-portions of the artery, indicating a mild stenosis, evaluated at 60%. The surrounding tissues were normal. These haemodynamic abnormalities remained stable for 4 months, but a retrospective study of the morphological patterns obtained in April showed a slight hypoechoic infiltration appearing around the artery which was initially not considered to be pathological.

The patient's blood pressure increased suddenly (180/100) in May 1995, and her weight increased by 2 kg, with a moderate serum increase in creatinine (172 µmol/l). A monitoring by US control showed a tight stenosis (estimated at 85%) with very high peak systolic velocities (3.5 m/s). A 4 cm hypoechoic mass was then detected around the artery at the level of the stenosis (Figure 1). There was no hydronephrosis. Angiography confirmed a tight, long stenosis with regular outlines and some neovascularization in the surrounding tissues and the hilum (Figure 2). Magnetic resonance imaging (MRI) gave a much clearer picture of the location and extent of the mass than did computed tomography (CT) because of its direct coronal slices and high contrast sequences (Figure 3).

Cervical, chest, and abdominal CT scans showed no...
EBV-associated B-cell lymphoma

Fig. 1. Colour Doppler image: the longitudinal scan revealed an area with colour aliasing, indicating a tight stenosis in the middle part of the graft artery, which was surrounded by a 4-cm diameter hypoechoicogenic mass.

Fig. 2. Angiography confirming the presence of a fusiform tight stenosis and showing some small tortuous vessels in the surrounding tissues, related to the neovascularization of the mass.

Fig. 3. MRI: frontal T1-weighted images after gadolinium injection. They clearly show the heterogeneous mass surrounding the graft pedicle and involving the hilum of the kidney, but sparing the iliac vessels.

Fig. 4. Allograft artery: arteriosclerotic fibrosis of the intima, and infiltration of the media and the intima by the lymphoid proliferation (HES.G = 5).

masses or adenopathy. There was no monoclonal gammapathy. Bone marrow aspiration revealed no abnormalities. The immunosuppressive treatment was stopped and transplant nephrectomy was performed in June 1995.

Gross examination. The kidney measured 11 x 6 cm and had a well-defined lesion (4 x 3.6 x 2 cm) lesion in the hilar area. The cut surface of the tumour appeared soft, whitish, partially haemorrhagic, and necrotic. The tumour surrounded the allograft hilar artery, which was stenosed and had compressed the allograft hilar vein and the ureter. The kidney parenchyma was macroscopically healthy.

Light-microscopy. The tumour was made up of a polymorphic lymphoid proliferation that was focally necrosed. Large lymphoid non-cleaved cells predominated, with features compatible with immunoblasts.
mainly of a lymphoid monoclonal B cell population
with diffuse, intense reactivity towards leucocyte
common antigen, MB2 and CD20, with lambda light-
chain secretions. Some large B cells were stained with
the EBV late membrane protein, and strong EBV
genome expression was found in many cells by molecu-
lar hybridization.

Cytogenetic features. A total of 10 metaphases was
analysed and karyotyped. All the metaphases con-
tained the same unaltered 46 XX.

These results confirmed the diagnosis of monoclonal
B cell lymphoproliferation, its association with the
Epstein–Barr virus, and its part in allograft artery
stenosis. The patient is doing well 6 months after graft
nephrectomy. She is on chronic haemodialysis and
there is no evidence of lymphoma.

Discussion

Post-transplant lymphoproliferative disorder (PTLD) is a well-documented complication of kidney trans-
plantation, but its exact incidence has not been accur-
ately determined. The incidence seems to be higher in
the USA than in Europe [1, 2]. The present report
describes the fifth patient to develop PTLD in the 24
years history of our programme (726 patients). This
incidence (0.6%) is similar to that reported recently by
a UK group [2].

Several factors contribute to the pathogenesis of
PTLD in immunosuppressed patients, including
impaired cellular immunity, chronic antigenic stimula-
tion by the allograft and immunosuppressive agents,
which may interfere with immune surveillance and
allow transformed lymphocytes infected with EBV to
grow without control by the immune system [3].

Although it is difficult to define the exact contribu-
tion of each individual agent, recent studies have implicated
triple therapy with cyclosporin–azathioprine–prednis-
one [4], prophylactic ATG [1], and OKT3 [5,6]. Our
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