Acute allograft glomerulopathy associated with CMV viraemia

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On day 44, the patient was re-admitted with right upper quadrant pain, malaise, and further deterioration in renal function (creatinine 349 μmol/l). Temperature was not raised; he was leukopenic (total leukocyte count 0.9 × 10⁹/l); his haemoglobin had dropped from 85 g/l to 76 g/l and platelets fell to 95 from 120 (× 10⁹/l); the blood film showed atypical mononuclear cells, giant platelets, and occasional fragments were reported. He had developed abnormal serum liver biochemistry (alanine aminotransferase, 297 U/l; gamma glutamyl transpeptidase, 379 U/l, alkaline phosphatase, 265 U/l). Consequently intravenous ganciclovir therapy was begun empirically for presumed CMV infection. The patient became dialysis-dependent. Allograft needle biopsy was performed, revealing intimal arteritis, but now also an acute allograft glomerulopathy (Figure 1c,d) with severe endothelial injury and PAS-positive capillary webs. No cytomegalic cells were identified on biopsy, and immunohistochemistry for CMV early antigens was negative. There were no glomerular red cell fragments or congestion and no arterial intimal oedema or intimal neofibrosis, making thrombotic microangiopathy unlikely. However, acute primary CMV infection was confirmed by detection of plasma CMV DNA by PCR, rapid detection of CMV early antigens, isolation of virus from peripheral white blood cells and from urine, and seroconversion to CMV antibody positive, including IgM antibody.

Ganciclovir was continued for 1 month, mycophenolate mofetil was discontinued, the dose of prednisolone was reduced, and tacrolimus dose was reduced from 0.1 mg/kg to 0.07 mg/kg. The patient continued to require haemodialysis for 2 months, before becoming independent of renal replacement therapy. The most recent allograft needle biopsy, 5 months after transplant, showed mild chronic allograft nephropathy; glomeruli revealed mild tuft retraction and increased mesangial matrix, without evidence of the acute allograft glomerulopathy. Fifteen months after transplant, plasma creatinine is stable.
at 270 μmol/l, he has no further symptoms of CMV disease, and his last CMV PCR assay was negative.

This case illustrates the association of a distinctive glomerular lesion—acute allograft glomerulopathy—with CMV viraemia [1,2]. Cytomegalic cells are not a feature of CMV-induced acute allograft glomerulopathy. CMV has been suggested to trigger this unusual glomerular injury indirectly, through interferon-stimulated upregulation of endothelial class I major histocompatibility complex antigens, which in turn stimulates the alloimmune response [3]. Acute allograft glomerulopathy is envisaged as the product of an altered form of acute rejection, targeting glomerular

and arterial endothelium, and precipitated by CMV, among other causes.

References