Atypical Presence of Antimyeloperoxidase Antibodies in 2 Transplanted Patients

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Dear Sir,

Transplanted kidneys can develop different types of vascular lesions which can be due to cyclosporin A (CyA) toxicity [1, 2] or to rejection manifestations [4]. We evaluated the sera of 54 transplanted patients for ANCA (antineutrophil cytoplasm antibodies). ANCA were tested with immunofluorescence (for cytoplasmic or perinuclear fluorescence pattern) and ELISA (Biocarb Diagnostics ‘Anti-Neutrophil Cytoplasmic Quantitative Kit’, Lund, Sweden). This kit detects antiproteinase 3 antibodies (PR3-Abs). Moreover ELISA was performed for antitymeperoxidase antibodies (MPO-Abs, Biocarb Diagnostics ‘Anti-Myeloperoxidase Quantitative Kit’, Lund, Sweden).

All the patients were negative for PR3-Abs. All the patients but 2 (patient 1 and 2) were negative for MPO-Abs. Patient 1 was transplanted in 1989 with a cadaveric kidney. His causal nephropathy was a type II (granular fluorescence) extracapillary proliferative glomerulonephritis (GN) (biopsy of 1986), without signs of necrosis or of vascular involvement, which led to end stage renal disease in 1986. His sera were collected during the dialysis period and after the transplantation. Sera of the previous period were lacking. A transplant biopsy performed in July 1989 showed signs of CyA acute toxicity. From the clinical point of view this patient has a stable renal function (serum creatinine 1.8 mg% since August 1989), absent proteinuria, no clinical or laboratory signs of vasculitis. Lymphocytotoxic activity against a selected panel was 30%.

Patient 2 was biopsied in 1970 for a nephrotic syndrome: membranoproliferative GN (MPGN) was detected. Hemodialysis was begun in 1978 and the patient received a cadaveric kidney in 1984. She had an acute rejection episode (on the 1st day) which was successfully treated. Her serum creatinine was stable (1.2-1.4 mg%) and proteinuria ranged from 0.1 to 0.4 g/day. This patient had no anti-HLA antibodies. Sera of this patient were collected since 1984; the most recent ones were clearly positive for MPO-Abs; the older sera showed borderline values.
Several speculations can be made from these 2 cases. In patient 1 the presence of MPO-Abs is compatible with the causal nephropathy, a rapidly progressive GN, even in the absence of overt clinical or histologic signs of vasculitis, as is now clearly demonstrated [3]. However MPO-Abs persisted during the dialysis treatment and the 3-year transplantation period, despite the associated immunosuppression. No signs of vasculitis appeared, nor of relapse of the initial nephropathy to which ANCA could be correlated. No signs of rejection are evident. The question arises as to whether the positive results are a consequence of the transplant situation itself, in particular of some lesions of the transplant vasculopathy [4], or of the treatment with CyA, which is also known to be responsible for vascular damage [1, 2]. However, both hypotheses disagree with the negative finding in all the other 52 patients tested. Patient 2 had a MPGN. The positive values of MPO-Abs found are unexplained. In this patient as well there is no correlation with the appearance of signs of vasculitis, of rapidly progressive GN, or of rejection. Neither of the 2 patients was submitted to a transplant biopsy, when the ANCA-positive data were detected, as there were no clinical or other laboratory reasons for this. However it seems justified to question whether the vasculopathy correlated to transplantation (secondary to CyA treatment, or to acute or chronic rejection) could be part of the ANCA-associated diseases.

Even if there is no logical explanation for ANCA-positive data in these 2 cases, our results seems important as they underline the non unequivocal significance of ANCA, in particular of MPO-Abs, with their possible inexplicable association with different pathological entities.

References