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Inadvertent cadaver kidney transplantation across the ABO barrier: a case report

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Dear Editors:

ABO histo-blood group is one of the most important transplantation systems due to the expression of ABO antigens on almost all cells in the body and due to the presence of natural antibodies [1].

When the kidney transplantation era started, several grafts were performed between ABO-incompatible subjects [2, 3, 4]. The results were so disappointing that, for many years, transplantation across the ABO barrier was considered a predictive factor for hyperacute rejection of the graft. As a matter of fact, the morphological changes observed in the explanted kidneys were comparable to those seen in intravascular thrombosis due to HLA alloantibodies binding to renal vascular endothelial cells.

In the subsequent years, the shortage of human organs for transplantation prompted clinicians to assess the possibility of crossing the ABO blood-group barrier using organs with a low expression of the incompatible antigen, such as A_2. In the 1970s, several clinical trials of kidney transplantation between ABO-incompatible individuals were carried out across the world [5, 6, 7]. Since these experiences, other isolated cases [8, 9, 10] and large series [11, 12, 13] have been reported.

Transplantation of kidneys with strong expression of incompatible A/B antigens was reported by Slapak et al. [14] and Alexandre et al. [15] who, in 1982, started a specific programme in Brussels. The patients that had received transplants required a more potent immunosuppression, often accompanied by splenectomy and plasmapheresis or immunoadsorption, to reduce A,B antibody titre [14]. Complete overviews and single-centre studies on ABO incompatibility in solid-organ transplantation have been published [16, 17, 18, 19].

In this letter we report on a patient of blood group B who was inadvertently given a kidney from a cadaver donor of blood group A_1.

In 1996 the patient, G.L., on dialysis since 1994 because of focal glomerulosclerosis, at 58 years of age entered the kidney waiting list of the North Italy Transplant programme (NITp). At the time of registration G.L. was reported to us as having an A Rh-positive blood type. The patient's HLA typing, performed by serology, was A2,3;B17,18; DR11,15. No history of previous blood components was reported.

On September 6th, 1997 the patient was selected for kidney transplantation according to the NITp algorithm, based on ABO identity, HLA compatibility, age matching and waiting time [18, 20], and was given a kidney from a donor typed as blood group A_1 and HLA-A2;B8,61;DR3, 11.

The immunosuppressive regimen of the patient consisted of tacrolimus

(5 mg × 2), azathioprine (100 mg), and methylprednisolone (from 12 mg to 4 mg in 2 months). The level of tacrolimus was 10–15 μg/l. Treatment comprised diuretic therapy to maintain urine output. On the 20th of September G.L. was dismissed from the hospital with a serum creatinine level of 211 μmol/l. Fourteen months after transplantation, renal function became worse, with a serum creatinine level of 270 μmol/l. Methylprednisolone was increased to 8 mg/day.

In January 1999 azathioprine administration was temporarily suspended because of leukopenia. On that occasion a further deterioration of renal function was observed. In April 1999 azathioprine was replaced by mycophenolate mofetil (MMF). A renal biopsy was carried out, and the histological examination revealed chronic allograft nephropathy. Retrospectively, the presence of C4d was investigated in the paraffin sections of the renal biopsy by an indirect immunoperoxidase technique, after antigen retrieval by pressure-cooking using a polyclonal anti-C4d antibody (Biomedica, Vienna, Austria). No C4d staining was detected in the peritubular capillaries.

The patient was administered one pulse of methylprednisolone (500 mg) and given MMF (1 g × 2), with a maintenance level of tacrolimus of 6 μg/l.

Between July and November 1999, an increase in creatinine level, proteinuria and hypertension, controlled by calcium antagonists, were observed.

In September 2000, G.L. returned to haemodialysis and the transplanted kidney was removed. The explanted kidney was submitted for pathological examination. At histology, features of chronic sclerosing allograft nephropathy were present. Very mild tubulitis, < 4 intraepithelial lymphocytes for tubular cross-section (according to the Banff 97 classification), was occasionally observed. Macroscopic and histological features were not consistent with acute rejection; therefore, molecular analyses for major infective agents and electron microscopy were performed. Polyoma virus analysis was negative.

Recently, G.L. has been re-admitted to the NITp kidney waiting list. From the documents provided by the clinicians, G.L. has blood group B. We tried to trace the error and discovered that the first blood group determination, performed in 1996 in the patient's hospital, was wrong.

We repeated the ABO grouping on a new, fresh, sample from the patient and on a frozen sample of DNA stored in our repository. Blood group B was confirmed, and anti-A antibody titre, performed on a serum sample stored before transplantation against random A_1 erythrocytes, was 1:8 (score 32). ABO typing of the cadaver donor was repeated with molecular biology, resulting in A_1.

To our knowledge, this is the first reported case of an adult patient given a kidney with a strong expression of incompatible A_1 antigen, which functioned for 3 years without splenectomy, plasmapheresis or immunoadsorption [19, 20] and administration of a potent immunosuppressive drug. Unfortunately, we cannot study in some detail the immunological status of this subject, using for example flow cytometry, since the error was discovered 3 years after transplantation. The fact that this ABO-incompatible kidney was not acutely rejected but survived and functioned mid-term may be due to the low titre of natural anti-A antibodies, detected in the pre-transplantation serum. The case presented here, also isolated, indicates that low-titre patients might not need intensive antibody removal therapy or immuno-absorption [18, 19, 21] and confirms the importance of reducing the pre-transplantation anti-A titre to 8 or below, by plasmapheresis, for a good outcome of ABO-incompatible kidney transplantation.

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