ACCOMMODATION OR EARLY CHRONIC HUMORAL REJECTION (CHR)?

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I: Introduction

Despite great progress in immunosuppressive therapy, late graft loss is still the main challenge in organ transplantation. The factors contributing to this problem may be immunological and/or non-immunological. The development of donor specific alloantibodies (DSA) plays an important role in late graft loss. This humoral participation in rejection can be indirectly shown by deposition of C4d in peritubular capillaries (PTC) of renal grafts. Rarely, grafts with normal renal function have C4d deposition (e.g. in ABO incompatible transplantation) with DSA in serum, suggesting that either antibody-mediated graft injury may be indolent, perhaps because of accommodation within the graft, or it could be an early stage leading to antibody-mediated chronic rejection.

Accommodation may be defined as an acquired state in which an organ resists to the consequences of DSA under conditions where rejection would be expected. Accommodation can be suspected if the graft shows no pathological changes, such as glomerulopathy, or arteriopathy, in the presence of normal renal function without proteinuria.

II: Case report

We present the case of a 28 year-old woman who underwent living-donor renal transplantation in 1997 due to kidney disease associated with May-Hegglin syndrome. In 1998, she was treated for acute cellular rejection with complete recovery of allograft function. In 2003, she underwent allograft biopsy which showed signs of calcineurin inhibitor toxicity associated, with diffuse C4d deposition in PTC. Circulating DSA were detected at the same time. In 2006, proteinuria and a rising creatinine developed, DSA were still present and C4d deposits were again demonstrated on the biopsy.

III: Conclusions

We show here a case which highlights the pernicious clinical effects of late de novo production of DSA after renal transplantation, and the importance of detecting C4d in renal PTC biopsy.

Detection of DSA with an apparently normal graft function may be either seen as a sign of “accommodation” or as an early stage of CHR.

Normal renal graft function does not mean absence of rejection, particularly if DSA in serum and C4d deposits are present.. When proteinuria and/or rising creatinine develop, it is usually a sign of chronic allograft glomerulopathy, due to CHR. For these reasons, monitoring of DSA in serum and protocol biopsies (C4d staining) are key to diagnose the early stages of CHR. This may be particularly important in the current era of “minimization” strategies.