

# Accommodation or early chronic humoral rejection ?

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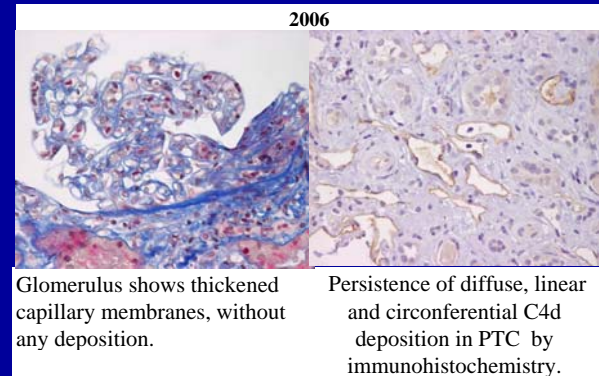
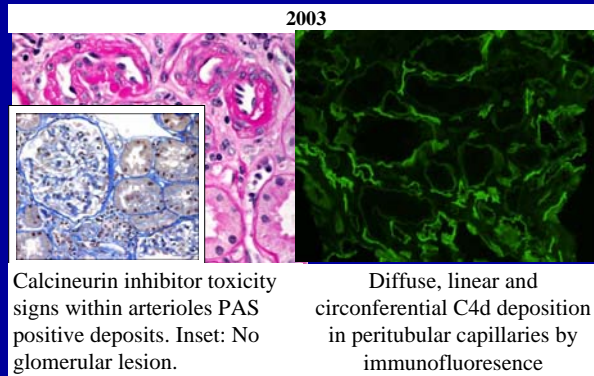
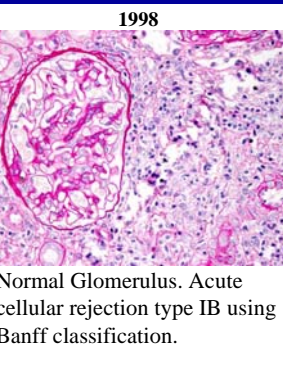
## I: Introduction

Despite 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) is crucial for this late graft loss. This humoral participation in rejection can be indirectly shown by deposition of C4d in peritubular capillaries of renal grafts. Rarely, grafts with a normal renal function have C4d deposition (e.g. in ABO incompatible transplantation), in presence of DSA in serum of these patients, suggesting either antibody-mediated graft injury may be indolent, perhaps because of accommodation within the graft, or a first step leading to an antibody mediated chronic rejection.

Accommodation may be defined as an acquired state in which an organ resists the assault of humoral rejection under conditions where rejection would be expected. A complete accommodation can be seen when the graft shows no pathological changes, such as glomerulopathy, or arteriopathy. At a cellular level, accommodation may be explained as a receptor desensitization to stimulation via multiple mechanisms such as internalization, downregulation, inactivation, or inhibition of the receptor.

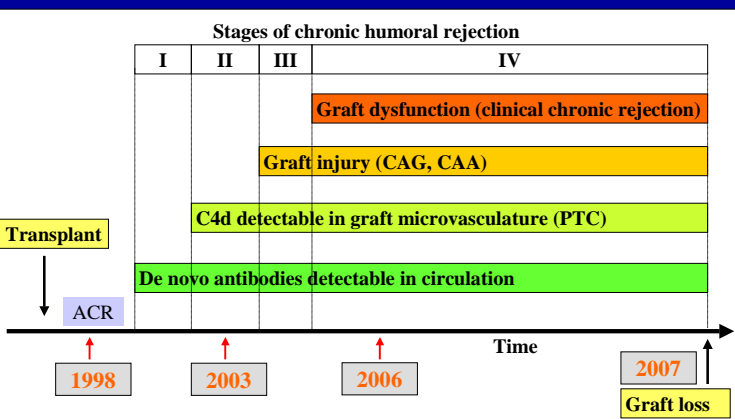
## II: Case report

We report here 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 cellular rejection with complete recovery of the renal function. In 2003, she underwent allograft biopsy which showed signs of calcineurin inhibitor toxicity associated with C4d deposition. Circulating DSA were detected at the same time. In 2006, proteinuria developed, DSA were still present and C4d deposits were again demonstrated on the biopsy.



	1998	2003	2006	2007
Acute cellular rejection	Yes	No	No	
Toxicity Calcineurin Inhibitor	No	Yes	Yes	
C4d deposits in PTC	Neg	Positif	Positif	
Chronic Allograft Glomerulopathy	No	No	Yes	
Proteinuria	0,18 g/d	0,3 g/d	5 g/d	3.8 g/d
Serum Creatinine	130 µmol/l	140 µmol/L	200 µmol/L	548 µmol/L (dialysis started in April)
B Cross-match	Neg	Positif	Positif	Not done
Donor Specific Antibodies	Neg	Positif: Anti-DR15	Positif: Anti-DR15	Positif (Luminex) : Anti-A31, A33, DR15, DR16
Treatment	Steroids boluses	30% reduction in Ciclosporine, No change in Prednisone	Switch to Tacrolimus, Prednisone, MMF (not tolerated) Rituximab x2 doses	Tacrolimus and Prednisone

## III: Discussion:



We show here a case demonstrating the pernicious effect of late de novo production of DSA after renal transplantation, and the importance of detecting C4d in renal peritubular capillaries on each renal graft biopsy.

Detection of DSA with an apparently normal graft function can be seen as a sign of "accommodation" or as an early step of CHR.

Normal renal graft function does not mean absence of rejection. When proteinuria develops, it is usually a sign of chronic allograft glomerulopathy, due to CHR. For these reasons, detection of DSA and protocol biopsies (C4d staining) are key to diagnose and prevent CHR.