Summary and conclusion

Acute humoral rejection (AHR), which occurs in up to 8% of kidney transplant recipients, is a significant cause of renal allograft dysfunction and loss ***(Bickerstaff et al, 2008)***.

Renal biopsy is the gold standard for diagnosis of acute rejection in renal transplant recipients (***Racusen et al, 2003***). Over the past decades, no well-defined criteria for the proper identification of humoral rejection episodes in the early or late post-transplantation period have been defined. Hence, antibody-mediated rejection episodes frequently remained undiagnosed and unclassified. Consequently, nearly all acute rejection episodes have been classified as 'cell mediated rejection' (***Nickeleit & Mihatsch, 2003***).

Currently, C4d is regarded as an immunological marker for a humoral-mediated response, not only by the pioneers in this field but also by many other centers which have included the use of C4d immunostaining during the work-up of allograft dysfunction (***Ranjan et al, 2008).***

The Banff (1997) classification was revised in 2007 incorporating morphological criteria, supported by immunopathological criteria, and serological evidence for acute humoral rejection ***(Cornell et al, 2008)***.

In this study we confirmed the important diagnostic role of immunofluorescent detection of complement degradation product C4d in peritubular capillaries in reclassification of acute humoral rejection cases according to the revised Banff schema (2007) and its role as a specific, reliable marker for antibody mediated rejection and confirmation of complement activation.

This study confirms a significant association between the histological criteria suspicious for acute humoral rejection according to the new revised Banff (2007) and the positive immunofluorescent staining for C4d. The most significant histopathological findings are the dilated, congested peritubular capillaries with neutrophilic inflammatory infiltrate (P-value=0.005) and the acute tubular necrosis (P-value=0.011), but not the presence or absence of glomerulitis, tubulitis, vasculitis or interstitial inflammatory infiltrate.

This study demonstrated the presence of histological features of cell mediated rejection in the form of tubulitis and interstitial inflammatory infiltration. This reflects the fact that the allograft rejection can be mediated by concomitant antibody and cell mediated immune mechanisms.

We also revealed the essential role of immonofluorescent detection of fibrinogen in vascular lesions as a specific marker for antibody mediated rejection due to activation of complement mechanisms and resultant neutrophil and macrophage chemotaxis and activation.

This study confirms the importance of fibrin detection as a major help in re-classification of acute humoral rejection cases according to the revised Banff grading system (2007) following its detection in blood vessels using the immunofluorescent technique. Its recognition in biopsy indicates a more aggressive form of antibody mediated rejection which necessitates specific lines of treatment.

The number of subsequent, multiple rejection episodes in relation to the acute humoral rejection diagnosis that was made by the peritubular detection of the complement split product C4d is higher than in cell mediated rejection cases, indicating the importance of early and accurate detection of acute humoral rejection cases with subsequent proper treatment, or else graft loss will be inevitable.

In the following study, the superior role of immunofluorescent technique over the immunohistochemical one is obvious, and it should be put into consideration to avoid missing acute antibody mediated rejection cases.

We demonstrated the importance of the use of appropriate anti-humoral rejection therapy for prevention of early graft loss or late complications.

So, from the present data we conclude the pivotal role of the C4d in detection and diagnosis of acute humoral rejection cases with the subsequent proper classification of graft rejection cases according to the Banff schema 2007.

It is also very obvious that C4d staining for graft rejection cases has a major role in modifying the protocol of treatment for better graft survival.

As for fibrinogen detection in vascular lesions using the immunofluorescent technique, it proves its importance as an essential step for detection of missed cases of fibrinoid necrosis which are specific for acute humoral rejection cases and were not confirmed by routine light microscopic staining. It also helped the precise re-classification of acute humoral rejection cases or appropriate treatment.