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Histologic Findings in Kidney Transplant Recipients: Three Years Study From Protocol Biopsies on 1 and 6 Months in Patients in R. Macedonia

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Introduction

A protocol biopsy of an allografted kidney has been introduced in many centers over the world in past years, to determine the presence of acute and chronic lesions in stable well-functioning allografts. Biopsy may also detect clinically unexpected lesions such as drug induced nephropathy, recurrent original disease, ischemic tubular injury. The information provided by different centers suggested that acute lesions tend to reach their maximum during the initial months after transplantation, and the incidence of chronic lesions is low during the first month, progressively increasing thereafter.[1] A significant number of the cases with acute rejection after kidney transplantation are low-grade forms according to Banff criteria[2], and so they are usually clinically silent and can be recognized at the time of biopsies. Early diagnosis of CAN as major cause of late renal allograft loss is important to determine treatment strategies. Protocol biopsies can also provide usuful information early in the evaluation process, often before clinical signs of CAN appear[3]. In Macedonia, most cases usually underwent biopsy at the time of graft dysfunction, but in the last three years the patients undergo to protocol biopsies at one and six months.

In this study we analyzed main histopathological changes in the protocol biopsies from grafts with stable renal function taken at one and six months using Banff Classification.

Materials and methods

A total of 28 paired biopsy specimens from allografted kidneys performed at 1 and 6 months, were diagnosed at the Institute of Pathology, Medical faculty, University of Skopje, during the period between October 2002 and April 2004. All specimens were sent in 10% formalin fixative, followed by a routine preparation for paraffin-embedded sections in our laboratory. Paraffin sections were stained with hematoxylin-eosin (HE), periodic acid-Schiff (PAS), Masson`s trichrome and silvermethenamine-PAS. Biopsies were considered adequate when they contained more than 7 glomeruli and at least one artery.

The immunosuppressive regimen consisted of methylprednisolone and Daclizumab as induction therapy, and cyclosporine, prednisolone and mycophenolate mofetil as maintenance posttransplant immunosuppression. Clinical values analyzed included age, sex, source of donor, serum urea/creatinine level and urine volume presence of proteinuria. Histological diagnosis was made according to the criteria of Banff working classification. In present study we included the cases with serum creatinine <200 mmol/L and proteinuria <1g/24 hours at the time of the first biopsy, which was defined as “stable” graft function.

Results

The mean age of the recipients was 35,2+/-8,3 years and male to female ratio was 3/1. The mean living donor age was 58,5+/-13,4 years. Histopathological diagnosis included six specimens (21,4%) with normal findings at 1 and 6 month biopsy. Borderline changes were found in 10/28 (35,7%) and 10/28 (35,7%) in the 1 and 6 month biopsies, respectively. Signs of acute rejection were found in 13/28 (46,4%) and 12/28 (42,8%) cases, at 1 and 6 months biopsy respectively: mild AR (5/28), moderate (6/28) and severe (2/28) in the first month, and mild 4/28 and moderate AR 12/28 in the sixth month.There was significant increase of CAN in the second allograft biopsy after six months. Hence, in the first biopsy we found mild digree of CAN in 14 specimens (50%) and moderate in 2 specimens (7,1%). On second biopsy CAN was detected in 23 cases (82%) (11 with mild CAN and 12 with moderate form of CAN).

It is of interest that in three cases there were found signs of cyclosporine nephrotoxicity, and two cases showed signs of recurrent disease (focal segmental glomerulosclersosis and diabetic glomerulopathy). Cyclosporine nephropathy showed typical arteriolopathy with nodular hyaline subintimal deposition.

When correlated these findings with the serum creatinine levels (sCr), we found significantly increased levels of sCr at 6 months after transplantation, while the calculated creatinine clearance (cCrcl) and proteinuria were significantly lower compared to the one month values for the repective group.

Discussion

We demonstrated histopathological findings of grafted kidneys, which clinically showed sufficient renal function at the time of biopsy. To select specimens we arbitrarily set up the criteria of serum creatinine less than 200 mmol/L and proteinuria less than 1g/24 hours at the time of the first biopsy, which was defined as “stable” graft function.

Our results showed presence of high percentage of BR and AR in allograft biopsies, that means they do not necessarily cause clinically recognizable graft dysfunction. Higher percentage of BR and SR in this study comparing to previous reports[5] might be due to the different sampling time for the biopsies, as well as to the lower number of patients included in the study. Study of protocol biopsies from stable grafts had revealed an unexpectedly strong

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correlation between the subsequent decline in renal function and the presence of acute histologic features such as tubulitis and lymphocytic infiltration; this gives some support to the concept of "subclinical acute rejection" in the pathogenesis of chronic graft damage or chronic allograft nephropathy (CAN)[3,4]. In favor of this concept is the significant increase of CAN in the second biopsy taken at 6 months after transplantation, at present study.

Findings of recurrent disease and cyclosporine nephrotoxicity are important because of the further treatment strategy of such patients.

In conclusion, protocol biopsies are valuable to determine presence of changes indicating acute or chronic rejection which impact on the evolution of renal allograft. They are also important in finding of other lesions that might compromise renal allograft function.

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