THE IMPORTANCE OF RENAL BIOPSY IN THE MANAGEMENT OF RENAL TRANSPLANTATION

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THE IMPORTANCE OF RENAL BIOPSY IN THE MANAGEMENT OF RENAL TRANSPLANTATION (Abstract): Renal biopsy remains the"gold standard'' for the diagnosis of renal allograft dysfunction. The aim of our study was to highlight the importance of renal biopsy in the management of allograft dysfunction (early diagnosis and therapeutic approach). Our study included 23 renal allograft biopsies from 20 patients. This retrospective study analyzed the demographic and clinical data, histological results and the evolution of renal function under the immunosuppressive regimens. Conclusions: the most frequently encountered histopathological patterns were humoral rejection, interstitial fibrosis and chronic cellular rejection. Patients under continuous treatment with cyclosporine developed chronic cellular reject more frequently; on the opposite, patients under continuous treatment with tacrolimus developed chronic humoral reject more frequently. **Keywords**: RENAL BIOPSY, ALLOGRAFT DYSFUNCTION, IMMUNOSUPPRESSIVE TREATMENT

The mechanisms responsible for the appearance of lesions in renal allograft are complex and include numerous multifactorial processes that are influenced by a variety of factors, both donor and recipient related, but also secondary to post-transplant events: ischemia-reperfusion injury, cellular and humoral immunity, viral and bacterian infections, or calcineurin inhibitors toxicity (1). For the diagnosis of allograft injury, clinical and paraclinical tests had been used, but the renal biopsy still remains „the golden standard" method (2).

The allograft biopsy is usually performed when cellular or humoral rejection is suspected. The main indicator for allograft dysfunction is represented by a rise in serum creatinine levels above the baseline values. One single abnormal value is not generally an indication, but on the other hand a rise of at least 25% above the baseline values represents an indication to perform such a biopsy (3).

Other signs of rejection, like inexplicable fever, edema, hypertension, eosinophilia, oliguria or anuria and proteinuria, are unable to predict this diagnosis in 30-50% of cases; as such histological confirmation is frequently necessary (4, 5, 6).

The aim of this study was to underline the importance of renal allograft biopsy (RAB) in the management of transplant pa-

tients from a single Renal Transplant Center.

MATERIAL AND METHODS

We analyzed all biopsies performed between in „Dr. C.I. Parhon" Dialysis and Transplantation Center, from 01.01.2007 to01.07.2012. A TRU-CUT 14 G needle and a BARD INSTRUMENTS biopsy pistol were used to perform RAB. All biopsy pieces were fixated in formaldehyde and later in paraffin. All sections had between 3 and 4 μm in thickness. We used HE, PAS and Masson Trichrome stain. For the interpretation of RAB the 2009 Banff Classification was used (7).

We also included in our analysis baseline demographic, clinical and therapy data of the patients, but also the evolution in renal function.

RESULTS

We included 23 biopsies from 20 patients that were from patients evaluated in our Transplant Centre.

A. General results

1. Age and sex – the age of patients was between 19 and 58 years (media 38.5 years);

2. The majority of biopsies were from young male patients (tab. I);

3. From the total of 20 patients, 17 had received the renal allograft from a living relative, while the rest from a cadaveric donor.

4. The median duration from the moment of transplantation till that of the biopsy was 7.05 years (between 1 and 15 years) (fig.1). The RAB was performed more frequently in patients with a transplant between 1 and 4 years.

5. Patients' co morbidities are presented in table II. Most patients had associated infectious and cardiovascular pathologies.

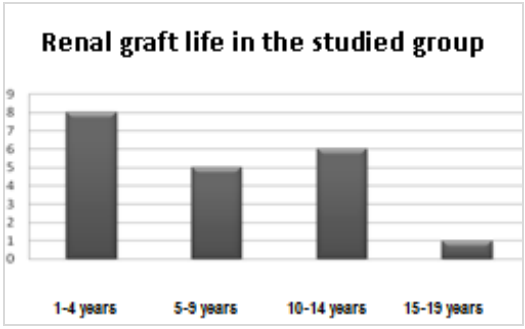

Fig. 1.The duration of renal transplant allografts.

TABLE I

The distribution of patients in regard with age and sex

		Number of patients	Number of biopsies
Sex	M	15 (75%)	18 (78.26%)
	F	5 (25%)	5 (21.73%)
Age intervals	15-24	3 (15%)	3 (15%)
	25-34	8 (40%)	10 (50%)
	35-44	6 (30%)	7 (35%)
	45-54	2 (10%)	2 (10%)
	55-64	1 (5%)	1 (5%)

TABLE II
Associated co morbidities

Associated pathology	Number of patients
HCV	**4**
VHB	1
CMV	13
PBKV	4
Hypertension	16

HCV – Hepatits C virus, HBV – Hepatits B virus, CMV - Citomegalovirus, PKBV – Polyoma BK virus.

4. **Pretransplant chronic kidney disease etiology –** in our study population the most frequent cause of CKD was chronic glomerulonephritis (12 patients); 3 patients had congenital renal abnormalities, while in the rest of patients the etiology was unknown.

5. **RAB indication –** six patients had a rapid rise in serum creatinine levels, the rest associating a more gradual decline in renal function with proteinuria > 1g/day.

B. Histopathological results

The most frequently histopathologies observed in our population were antibody mediated rejection (4 cases), interstitial fibrosis with tubular atrophy (3 cases) and T cell mediated rejection (3 cases) – see Table 3.

C. Post biopsy complications

Two patients had complications post RAB, and only case it was severe (subcapsular hematoma that later spontaneously remitted).

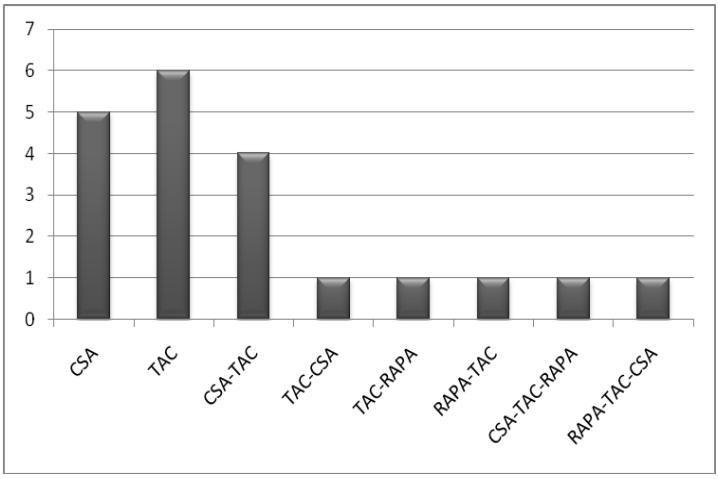

Fig. 2. Immunosuppression schemes in the study group:
CSA – Continuous therapy with Cyclosporine A. **TAC** – Continuous therapy with Tacrolimus. **CSA – TAC**: Cyclosporine – Tacrolimus switch. **TAC-CSA**: Tacrolimus – Cyclosporine switch. **TAC-RAPA**: Tacrolimus – Rapamycine switch.

D. Immunosupressive regimens

All regimens were based on three immunosupressives: prednison, myco-phenolate and either a calcineurin inhibitor (cyclosporine A (CSA) or tacrolimus (TAC)) or rapamycin (RAPA). The distribution of immunospressive regimens is presented in figure 2. In the observation period, most

patients remained on a calcineurin inhibitor (CSA or TAC) with a good evolution.

The modification of therapy was most frequently performed for chronic degradation of renal function (in the cases with CSA), diabetes (in the cases with TAC) or proteinuria (in the cases with RAPA).

Patients who had a CSA based regimen were more likely to develop chronic cellular rejection, while those with a TAC based regimen were more likely to develop chronic humoral rejection (tab. IV).

TABLE III
Histopathological results

Diagnostic	Number	Percentage (%)
Antibody mediated rejection	4	17.39 %
T cell mediated rejection	3	13.04 %
Interstitial fibrosis with tubular atrophy	3	13.04%
Non-diagnostic	3	13.04 %
Chronic allograft glomerulopathy	2	8.69 %
Borderline lesions	2	8.69 %
Virus infection	2	8.69 %
Chronic interstitial nephritis	2	8.69 %
Glomerulosclerosis	1	4.34 %
Calcineurin inhibitor toxicity	1	4.34 %

TABLE IV
Histopathological modifications according to the immunosupressive regimen

	CSA-TAC	TAC-CSA	TAC-RAPA	RAPA-TAC	CSA-TAC-RAPA	RAPA-TAC-CSA
T cell mediated rejection	**1**					
Interstitial fibrosis with tubular atrophy	**2**					
Borderline			**1**		**1**	
Calcineurin inhibitor toxicity	**1**					
Antibody mediated rejection	**1**					
Virus infection		**2**				
Chronic interstitial nephritis				**1**		**1**

DISCUSSION

The prevalence of end-stage chronic kidney disease is rising worldwide. At this moment there are 3 renal replacement therapies: peritoneal dialysis, hemodialysis and renal the quality of life and survival with the lowest long-term costs.

RAB represents the most sensitive instrument for detecting the cause of renal allograft dysfunction.

This paper underlines the significance of RAB for the management of a renal transplant patient. We retrospectively evaluated the histopathological results of all RAB performed in „Dr. C.I. Parhon" Dialysis and Transplantation Center in a five years period (01.01.2007 - 01.07.2012). There were only 23 biopsies from 20 patients.

The 4 cases with humoral rejection were diagnosticated at 1, 2, 7 months and 13 years after renal transplantation. After the treatment (all cases received 3 plasmapheresis, 2 patients also i.v. Imunoglobuline) there was amelioration in 3 cases. In the other case (the patient transplanted 13 years ago) there was an initial stabilization of serum creatinine levels, but he later returned to hemodyalisis.

In the three cases with cellular rejection, the evolution after methylprednisolone pulse therapy was favorable in all cases.

In the observation period, there was a 100% patient survival rate and a 95% renal allograft survival rate.

CONCLUSIONS

1. This study highlights the importance of RAB in the evaluation and management of renal transplant recipients.

2. RAB is of utmost importance in the clinical and therapeutical decisions, allowing medical practitioners to:

- identify and differentiate chronic or acute lesions in the allograft;
- initiate appropriate measures to stop or delay the progression to evident dysfunction and subsequent loss of the renal allograft.

3 . In our study the most frequent histopathological findings were antibody mediated rejection, followed by interstitial fibrosis with tubular atrophy and chronic cellular rejection;

4. Patients on continuous CSA treatment had a higher incidence of chronic cellular rejection, while those on continuous TAC treatment had a higher incidence of humoral rejection.

5. Post RAB complications have been rare, making this procedure a safe method of investigation kidney allograft dysfunction.

6. During the 5 years of the study, there was a 100% patient survival rate and a 95% renal allograft survival rate.

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