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Original Article

Histopathological evaluation of percutaneous renal biopsies: A single center experience

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Abstract

Aim: The aim of this study was to examine the indications, demographic features and histopathological diagnosis category of renal biopsies evaluated at the Pathology Laboratory of the University of Health Sciences Diyarbakır Gazi Yasargil Training and Research Hospital.

Materials and Methods: The information of 190 patients who underwent percutaneous renal needle biopsy between July 2017 and February 2020 was obtained from the approved final pathology reports.

Results: 190 biopsies were performed. 60% (n=114) and 40% (n=76) of the biopsies were native and transplant, respectively. 59.5% of the patients were male. Four of the patients were under 18 years. The mean ages of the native and transplant biopsy groupes were 37±14, and 34±14, respectively. Proteinuria was the most common biopsy indication (79.5%).Nonspecific changes were the most common diagnosis of the native biopsies. It was followed by focal segmental glomerulonephritis (FSGS), membranous glomerulonephritis (MGN), and IgA nephritis (IgAN). The most common secondary cause of glomerulonephritis was lupus nephritis. Acute cellular rejection was the most common diagnosis of the transplant renal biopsies.

Conclusion: Proteinuria was identified as the most common indication for biopsy. In the present study, the primary glomerular disease was FSGS while the secondary was lupus nephritis. With electron microscopic examination, it might be possible to decrease the number of patients who cannot be definitively diagnosed histomorphologically.

Keywords: Histopathological evaluation; glomerulonephritis; renal biopsy

INTRODUCTION

Renal biopsy is a very important diagnostic method that is often preferred in the diagnosis of native and transplant kidney diseases. It is the gold standard method for the definitive diagnosis of some diseases. In addition, it makes an important contribution to monitoring the disease and determining the treatment protocol (1-3). Percutaneous renal needle biopsy is a method performed by means of a full or semi-automatic needle accompanied by ultrasonography. Renal biopsy has indications such as proteinuria, hematuria, and acute kidney injury (4).

In some developed countries, there are national kidney biopsy registry systems and, it can provide statistical data of kidney diseases (5-8). It can provide better recognition, prevention and better treatment of the diseases. The aim of our study was to evaluate the native and transplant percutaneous renal needle biopsy results in terms of demographic, histopathological and also biopsy indications.

MATERIALS and METHODS

190 patients who underwent non-neoplastic native and transplant kidney biopsies at the Medical Pathology Laboratory of University of Health Sciences Diyarbakir Gazi Yasargil Training and Research Hospital between July 2017 and February 2020 were included in this retrospective descriptive study. The information of the patients was obtained from approved final pathology reports.

The kidney biopsy procedure was performed by an experienced radiologist. In native biopsies, patients were processed in the prone position, in transbiopsies, in the supine position. General or sedation anesthesia was not used in any patient. Prilocaine hydrochloride (priloc) was used as a local anesthetic. After local anesthesia,

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a small incision was made on the skin and the skin-subcutaneous soft tissues were passed through with a 17G coaxial needle and the kidney was placed in the tissue at a tangent angle from the lower pole cortex. The inner needle (stylet) was removed, an automatic biopsy gun with an 18G needle was placed in the cannula and biopsy samples were taken. Absorbable hemostatic gelatin sponge (spongostan) was used for bleeding control. In the majority of the cases, an expert pathologist accompanied the radiologist during the biopsy procedure for tissue adequacy assessment. Biopsy samples were provided to reach the pathology laboratory within 15-20 minutes. Firstly, tissue 2-4 mm in length containing glomeruli was allocated for immunofluorescence examination. It was kept at (-50)^{0}C for 24 hours in the frozen device (Shandon/Cryotome SME/USA). Each remaining tissue was processed separately and paraffin blocks were obtained. For light microscopic examination, tissues were cut at 3 micron thickness. Positively charged slides were used. There were at least 3 tissue sections on each slide. A total of 12 slides were obtained for native biopsy and 16 slides for transplant biopsy. Sections were obtained for 5 slides (1,4,5,8,9) H&E, 2 slides (2,6) JMS, 1 slide PAS (3), masson trichrome (7), Congo Red (10) Crystal violet (11). Sections were routinely obtained for C4d in native biopsies, and for C4d, SV40, CMV, LCA, CD4, CD8 in transplant biopsies in immunohistochemical study. Slides were kept in the oven for 90 minutes, at (+70)^{0}C for deparaffinization. The slides were then stained and sealed with lamella using the appropriate sealant. Immunohistochemical and immunofluorescent staining was performed with ready-to-use antibodies in the fully automated Ventana/ Benchmark XT/USA device. Immunofluorescence staining was performed in the dark area, and after staining, the slides were closed with a lamella using (DAKO/ Flurencence Mounting Medium/ USA) liquid and kept in dark at (+4)^{0}C for examination. Anti IgG/IgA/IgM/C3/C1q/Albumin/Fibrinogen /Kappa and Lambda light chain antibodies were used for immunofluorescence examination (Olympus BX53/U-LH100HG/JAPAN). Presence of at least 10 glomeruli was considered sufficient in microscopic examination, presence of 7-10 glomeruli was suboptimal, and presence of less than 7 glomeruli was considered as insufficient material.

Cases that could not be diagnosed with light and immunofluorescent microscopic examination findings, requiring electron microscopic examination (minimal change disease-unsampled FSGS distinction, cases with nonspecific immunofluorescent staining etc.), ischemic changes, and cases with mild microscopic changes were evaluated under the group of nonspecific changes as pathologic diagnosis. Transplant biopsy evaluation was performed according to the most recent Banff criteria (9). Banff criteria were determined for the evaluation of trans cases. These criteria are updated every 2 years with international Banff meetings.

Ethics committee approval numbered 03/07/2020-502 was obtained from the ethics committee of Health Sciences University Diyarbakİr Gazi Yasargil Training and Research Hospital.

Statistical Analysis

SPSS version 22.0 (SPSS Inc, Chicago, IL, USA) was used for statistical analysis. Continuous variables were given as percentage, mean and standard deviation (mean ± SD). Demographic data included the age, gender, native / transplant information. The symptoms, laboratory results, clinical preliminary diagnosis information of patients were excluded in the present study.

RESULTS

60% of biopsies were native renal biopsies while 40% were transplant renal biopsies. All of the native renal biopsies (n = 114) and 94.7% (n = 72) of transplant renal biopsies (n = 76) belonged to the patient group of 18 years and older. 59.5% of the patients were male, the mean age was 37 ± 14 year in the native kidney group and 34 ± 14 year in the transplant kidney group. The demographic results of the patients are summarized in Table 1.

Table 1. Demographic characteristics of native and transplant biopsies

	Total number of patients = 190 (100%)	Total number of female patients = 77 (40.5%)	Total number of male patients = 113 (59.5%)	Age Mean±SD (year)
Native Biopsy	114 (60%)	55 (48.2%)	59 (51.8%)	37±14
Transplant Biopsy	76 (40%)	22 (28.9%)	54 (71.1%)	34±14

Table 2. Histopathological characteristics of native biopsies

Diagnosis	Number of Patients	Percentage
Nonspecific changes	24	21.0%
Focal segmental glomerulosclerosis (FSGS)	22	19.3%
Membranous Glomerulonephritis (MGN)	21	18.4%
IgA nephritis (IgAN)	15	13.2%
Lupus nephritis	9	7.8%

Renal Amiloidosis	5	4.4%
AA Amyloidosis	4	3.5%
AL Amyloidosis	1	0.9%
C3 glomerulopathy	3	2.6%
Chronic kidney disease	3	2.6%
Chronic tubulointerstitial nephritis	3	2.6%
Kidney results related to Fabry disease	2	1.8%
Acute tubular necrosis	1	0.9%
Acute tubulointerstitial nephritis	1	0.9%
ANCA associated pauci immune glomerulonephritis	1	0.9%
Results compatible with C4 glomerulopathy	1	0.9%
Chronic active tubulointerstitial nephritis	1	0.9%
Thrombotic Microangiopathy (TMA)	1	0.9%
Insufficient material	1	0.9%
Total	114	100%

As it can be seen in Table 2, there are nonspecific changes in the histopathological diagnosis category of patients undergoing native biopsy most commonly, with a rate of 21%, which could not achieve definitive diagnosis with light and immunofluorescent microscopic examination results. The most common diseases were Focal segmental glomerulosclerosis (FSGS) (19.3%), Membranous glomerulonephritis (MGN) (18.4%), IgA nephritis (IgAN) (13.2%), lupus nephritis (7,8%) and Amyloidosis (4.4%), respectively. Diagnoses with less numbers and rates are given in Table 2.

Acute cellular rejection (in which borderline group was also added) was reported 33.2% of the transplant biopsies. This was followed by nonspecific changes (15.8%), calcineurin inhibitory toxicity (15.8%), FSGS (10.5%), human polyomavirus, BK virus (BKV) nephropathy (3.9%). Diagnoses with less numbers and rates are given in Table 3.

Biopsy indications of 190 patients are summarized in Table 4. Approximately half of the cases performed due to reasons such as non-nephrotic proteinuria and high creatinine accompanying proteinuria. This was followed by nephrotic proteinuria (30.0%) and non-proteinuria (20.5%), respectively. In total, 79.5% of the biopsy indication was the presence of proteinuria.

Table 3. Histopathological features of transplant biopsies

Diagnosis	Number of Patients	Percentage
Acute cellular rejection	25	33.2%
Borderline	7	9.3%
Type 1a	6	8.0%
Type 1b	2	2.6%
Type 2a	9	12.0%
Type 2b	1	1.3%
Nonspecific changes	12	15.8%
Toxicity results of Calcineurin Inhibitor (CNI)	12	15.8%
Focal segmental glomerulosclerosis (FSGS)	8	10.5%
BK virus nephropathy	3	3.9%
Acute tubular necrosis (ATN)	2	2.6%
IgA nephritis (IgAN)	2	2.6%
IgA nephritis + Membranous Glomerulonephritis	1	1.3%
Thrombotic Microangiopathy (TMA)	1	1.3%
AA Amyloidosis	1	1.3%
C3 glomerulopathy	1	1.3%
Active humoral rejection + C3 nephropathy	1	1.3%
Active humoral rejection	1	1.3%

Active humoral rejection + Acute cellular rejection type 2a	1	1.3%
Acute tubulointerstitial nephritis	1	1.3%
Chronic active humoral rejection	1	1.3%
Chronic active cellular rejection type1b	1	1.3%
Chronic active cellular rejection type1b + Chronic active humoral rejection	1	1.3%
Normal renal tissue	1	1.3%
Total	76	100%

Table 4. Biopsy indication analysis in cases

Indication	Number of cases	Percentage
Nephrotic proteinuria	57	30.0%
Non-nephrotic proteinuria ± other conditions	94	49.5%
Non-proteinuria causes	39	20.5%
Total	190	100%

DISCUSSION

The first renal biopsy assessment started in July 2017 in our hospital. Since our hospital also provides health services to the surrounding provinces, the results of renal biopsy of our region were revealed with this study for the Southeastern Anatolia region. Transplant and native biopsy patients were examined individually, as they were two different populations in terms of clinical follow-up and diseases. Since our hospital serves the adult patient population to a large extent, all patients except for 4 transplant patients were in the adult age group.

Percutaneous renal needle biopsy is a very important method in the diagnosis and management of kidney diseases. One study suggested that histomorphological results might change treatment protocols by 80% (10). Today, percutaneous renal biopsy is accompanied by new technological equipment, which reduces the risk of serious complications (11,12), therefore, it is often preferred. Complications such as pain, hematoma, macroscopic hematuria, major hemorrhage and arteriovenous fistula formation were reported to be observed in several studies (13-15). In our study, no major complication was observed in any of our patients during their post-biopsy follow-up. We think that it is due to the use of absorbable haemostatic gelatin sponge (spongostan) and the effectiveness of the method used in the biopsy procedure.

There are differences in studies analyzing renal biopsy indications in the literature, but proteinuria was identified as the most common indication (5-8). Our study was compatible with the literature and the most common indication was proteinuria with a rate of 79.5%. The indication of kidney biopsies has been reported as nephrotic proteinuria between 31.5-64.5% in Turkish patients (16-18). This rate was 30% in our study and it was below the percentage stated above. It is thought that this may have been caused by the low number of pediatric patients.

A study from Australia reported that IgA nephritis and FSGS were most common among primary glomerulonephritis in adults. (19). Another study from Romania identified the most common primary glomerulonephritis as Membranoproliferative glomerulonephritis (MPGN) (29.4%), followed by IgA nephritis (28.9%), FSGS (11.5%), Membranous glomerulonephritis (MGN) (11,2%) (20). A study from Serbia identified MGN (28.7%) as the most common, followed by FSGS (21). Another study found IgA nephritis (34.9%) as the most common and MGN (11.6%) as the second most common (22). The reason for finding different results in these studies is not completely known. It is thought that this difference can be explained by regional and genetic variability of kidney diseases and differences in biopsy evaluation facility (presence of electron microscopy, device that performs optimal staining and use of quality material and staining kit), method and experience. In the present study, when the pathology results of patients undergoing native biopsy were examined, the most common diagnostic category was nonspecific changes (21%), followed by FSGS (19.3%), MGN (18.4%) and IgA nephritis (13.2%). Considering the presence of Minimal Change Disease - unsampled FSGS distinction not performed or unsampled FSGS interpretation performed, which were evaluated within the category of nonspecific changes, it is thought that the rate would increase in favor of FSGS. In addition, Lupus nephritis (7.8%) and amyloidosis (4.4%) were the most common diseases in our study in terms of secondary glomerulonephritis, respectively. In one study, FSGS, MGN and IgA nephritis were the most common primary glomerulonephritis, respectively (18). The frequency order in terms of primary glomerulonephritis seems to be partially compatible with the present study. The causes of secondary glomerulonephritis vary in some different studies. Some studies found amyloidosis (23,24) as the most common while other studies found lupus nephritis (16,17) as the most common. Lupus nephritis is shown to be the most common secondary cause of glomerulonephritis (5-7) in countries such as America, Asia, and Europe, which represent part of the patient population. In the present study, lupus nephritis is the most common cause of secondary glomerulonephritis and is compatible with some of the studies above.

Transplant renal biopsies are evaluated according to the criteria determined by Banff and reviewed every two years. In a study conducted in our country in 2018, nonspecific changes (63.3%) were ranked the first in the transplant

biopsy diagnosis, followed by acute antibody-mediated rejection (12.6%) and acute cellular rejection (3.3%) (24). In our study, acute cellular rejection (with the borderline group added) was in the first place (33.2%). This was followed by nonspecific changes (15.8%), calcineurin inhibitory (CNI) toxicity (15.8%), FSGS (10.5%), BK nephropathy (3.9%).Nonspecific changes in both native and transplant biopsies , constituted 18.9% of all cases. These patients were reported with histomorphological interpretation and some diagnoses were highlighted. Although there were no definitive diagnosis, some diseases eliminated and important information were provided with respect to type and grade of histomorphologically interstitial inflammation, interstitial fibrosis-tubular atrophy rate, number and rate of global sclerosis as well as treatment selection and dosage. However, making a definitive diagnosis of renal diseases will ensure that patients receive the most accurate and effective treatment. Most of the diseases in the category of nonspecific changes can be diagnosed with electron microscopic examination and effective and appropriate treatments can be administered. In addition, actual disease distributions can be revealed.

Lack of detailed clinical data, no pediatric patients in native biopsy group, single centered and retrospective design was some of the limitations of this study.

National renal biopsy registry system is essential as it provides important informations about kidney diseases. Sufficient equipment for optimal kidney biopsy and a joint approach of experienced nephrologist and nephropathologist are required for optimal evaluation. In our country, sufficient hospital infrastructures should be established in every province and the experienced nephrologist and nephropathologist inadequacy should be filled. Thus, patients should be able to have a biopsy within the indication and be diagnosed and treated as soon as possible. End-stage renal failure, dialysis and complication rate can thus be reduced, as a result of which a great contribution will be made to the national economy.

CONCLUSION

The most common indication for renal biopsy in our center is proteinuria. In the present study, the most common primary glomerular diseases were FSGS, MGN and IgA nephritis while secondary glomerular diseases were lupus nephritis and amyloidosis. The presence of the renal biopsy national registry system will enable the researchers to reach more accurate information about kidney diseases and to treat these diseases faster and more effectively. Electron microscopic examination is needed for the definitive diagnosis of some renal diseases.

Competing interests: The authors declare that they have no competing interest.

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REFERENCES

1. Printza N, Bosdou J, Pantzaki A, et al. Percutaneous ultrasound-guided renal biopsy in children: A single centre experience. Hippokratia 2011;15:258-61.
2. Pirani CL: Evaluation of kidney biopsy specimens, In Tisher CG, Brenner BM (eds): Renal Pathology: With Clinical and Functional Correlations (2nd ed). Philadelphia, PA: Lippincott 1994;85-115.
3. Fuiano G, Mazza G, Comi N, et al. Current indications for renal biopsy: A questionnaire-based survey. Am J Kidney Dis 2000;35:448-57.
4. Piskinpasa S, Dede F, Akoglu H, et al. Clinicopathological Evaluation of the Kidney Biopsies: Our Center's Experience. Turk Neph Dial Transpl 2012;21:167-72.
5. Rivera F, López-Gómez JM, Pérez-García R. Spanish Registry of glomerulonephritis: Frequency of renal pathology in Spain. Nephrol Dial Transplant 2002;17: 1594-602.
6. Rychlík I, Jancová E, Tesar V, et al. The Czech registry of renal biopsies. Occurrence of renal diseases in the years 1994-2000. Nephrol Dial Transplant 2004;19: 3040-9.
7. Schena FP: Survey of the Italian registry of renal biopsies. Frequency of the renal diseases for 7 consecutive years. The Italian Group of Renal Immunopathology. Nephrol Dial Transplant 1997;12: 418-26.
8. Heaf J, Løkkegaard H, Larsen S. The epidemiology and prognosis of glomerulonephritis in Denmark 1985-1997. Nephrol Dial Transplant 1999;14:1889-97.
9. Haas M, Loupy A, Lefaucheur C, et al. The Banff 2017 Kidney Meeting Report: Revised diagnostic criteria for chronic active T cell–mediated rejection, antibodymediated rejection, and prospects for integrative endpoints for next-generation clinical trials. Am J Transplant 2018;18:293-307.
10. Richards NT, Darby S, Howie AJ, et al. Knowledge of renal histology alters patient management in over 40% of cases. Nephrol Dial Transplant 1994;9:1255-9.
11. Korbet SM. Percutaneous renal biopsy. Semin Nephrol 2002;22:254-67.
12. Stratta P, Canavese C, Marengo M, et al. Risk management of renal biopsy: 1387 cases over 30 years in a single centre. Eur J Clin Invest 2007;37:954-63.
13. Eiro M, Katoh T, Watanabe T. Risk factors for bleeding complications in percutaneous renal biopsy. Clin Exp Nephrol 2005;9:40-5.
14. Hergesell O, Felten H, Andrassy K, et al: Safety of ultrasound-guided percutaneous renal biopsy-retrospective analysis of 1090 consecutive cases. Nephrol Dial Transplant 1998;13:975-7.
15. Manno C, Strippoli GF, Arnesano L, et al. Predictors of bleeding complications in percutaneous ultrasound-guided renal biopsy. Kidney Int 2004;66:1570-7.

16. Sayarlioglu H, Erkoc R, Topal C, et al. Epidemiology of glomerulonephritis in the City of Van: Pathological findings of 129 cases. Turk Neph Dial Transpl 2005;14: 23-5.
17. Ecder SA, Kılıçaslan I, Ecder T, et al. Clinicopathological evaluation of five hundred and thirteen kidney biopsies. İst Tıp Fak Derg 2005;68:43-5.
18. Hur E, Taskin H, Bozkurt D, et al. Adult native renal biopsy experience of Ege University for 12 consecutive years. BANTAO J 2010;8:22-9.
19. Briganti EM, Dowling J, Finlay M, et al. The incidence of biopsy-proven glomerulonephritis in Australia. Nephrol Dial Transplant 2001;16:1364-67.
20. Covic A, Schiller A, Volovat C, et al. Epidemiology of renal disease in Romania: a 10 year review of two regional renal biopsy databases. Nephrol Dial Transplant 2006;21:419-24.
21. Naumovic R, Pavlovic S, Stojkovic Det al. Renal biopsy registry from a single centre in Serbia: 20 years of experience. Nephrol Dial Transplant 2009;24:877-85.
22. Wirta O, MustonenJ, Helin3 H, et al. Incidence of biopsy-proven glomerulonephritis. Nephrol Dial Transplant 2008;23:193-200.
23. Gurel A, Aygen B, Duzenci D, et al. Experience of Our Nephrology Clinic on Ultrasound Assisted Percutaneous Kidney Biopsy in Adults on Three Year Period: A Clinicopathologic Evaluation 2012;26:107-9.
24. Tekin E, Diniz G, Karadeniz T, et al. Histopathological profile of kidney biopsies: Single center, four years experience. Tepecik Egit ve Arast Hast Dergisi 2018;28:181-6.