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Discrepancies between clinical and pathological findings seen at renal biopsy in rheumatological diseases

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SUMMARY

Objective. Renal biopsy contributes to the diagnosis, follow-up, and treatment of many rheumatic conditions. This study assessed the diagnostic role and safety of renal biopsies in a tertiary rheumatology clinic.

Methods. Renal biopsies performed between June 2020 and December 2022 were screened, and demographic, clinical, histopathological, and safety data were collected from patient records.

Results. In this study, 33 males and 38 females were included. Except for 1 patient who received acetylsalicylic acid, antiaggregant, and/or anticoagulant drugs were stopped before the biopsy. Complications included a decrease of hemoglobin in 8 patients (11.3%) and microscopic hematuria in 40 patients (56.3%). Control ultrasonography was performed in 16 patients (22.5%), and a self-limiting hematoma was found in 4 of them (5.6%) without additional complications. While less than 10 glomeruli were obtained in 9 patients (9.9%), diagnosis success was 94.4%. Histopathological data were consistent with one of the pre-biopsy diagnoses in 54 of 67 cases (80.6%) but showed discrepancies in 19.4% (n=13) of patients. A repeat biopsy was performed in 7 patients for re-staging or insufficient biopsy.

Conclusions. Renal biopsy significantly contributes to rheumatology practice, especially in patients with complex clinical and laboratory findings or in whom different treatments can be given according to the presence, severity, and type of renal involvement. Although the possibility of obtaining insufficient tissue and the need for re-staging and repeat biopsy in the follow-up might be expected, complication risk does not seem to be a big concern. Renal biopsy often evidenced discrepancies between pre-biopsy diagnosis and histopathological findings.

Key words: *Renal biopsy, vasculitis, interventional radiology, renal pathology, complications.*

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INTRODUCTION

Rheumatologists deal with a wide spectrum of diseases exhibiting multi-systemic findings. The presence of renal involvement is critical for the prognosis of rheumatic diseases, especially regarding its type and severity (1-8). Hematuria, pyuria, proteinuria, and impairment of renal functions such as a decline in glomerular filtration rate or rise in serum creatinine/urea level are clues for renal involvement (9). In addition to the quantitation of these markers, renal biopsy is used as a diagnostic method due to the lack of a specific non-invasive diagnostic test. However, there is no standardization for whom and when to apply it, and pre- and post-procedure follow-up and complications are important concerns. In this study, we aimed to analyze the renal biopsies performed in our center in terms of their contribution to diagnosis and treatment, safety, and complications.

MATERIALS AND METHODS

Study design

This study was designed as a descriptive, retrospective, single-center study. Information related to demographics, clinical findings, laboratory parameters, pre- and post-biopsy diagnosis and treatments, histo-

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pathological findings, complications, and sufficiency data of biopsies was collected from the study participants' charts.

Participants and renal biopsy indications

All consecutive patients who underwent renal biopsy in our rheumatology clinic between June 2020 and December 2022 were included in the study group. Exclusion criteria comprised patients who were followed in our center but underwent renal biopsy in another center and patients whose clinical and laboratory data were insufficient to analyze. In our cohort, there were a total of 81 patients who underwent renal biopsy at least once during follow-up. However, 6 of them were admitted to our clinic after the performance of a renal biopsy at another center, and 4 were excluded because of insufficient data.

For patients with connective tissue diseases or systemic vasculitis, including systemic lupus erythematosus (SLE), Sjögren's disease, and antineutrophil cytoplasmic antibodies (ANCA) - associated vasculitis (AAV), proteinuria higher than 0.5 g/day or progression in renal function tests were the main indications to investigate renal involvement. For leukocytoclastic vasculitis, Henoch Schönlein purpura, spondyloarthropathies (SpA), and familial Mediterranean fever (FMF) patients, proteinuria, hematuria, or progressive decline of renal functions tests were the main indications to investigate AA amyloidosis, immunoglobulin (Ig) A nephropathy, analgesic nephropathy, and other renal involvements. For other patients, including rheumatoid arthritis (RA) patients or patients with undifferentiated or non-specific findings suggesting renal involvement associated with rheumatologic disorders and hypertension/diabetes mellitus, renal biopsy was indicated to differentiate primary renal disease such as diabetic or hypertensive nephropathy, membranous glomerulonephritis, or renal involvement of the rheumatologic disease. The patients' clinical diagnoses were assessed considering both signs and symptoms and laboratory findings, including serologic and genetic tests. Among them, proteinase 3 and myeloperoxidase ANCA for AAV, anti-nuclear antibodies, anti-double stranded DNA, and extractable nuclear antigen panel tests for SLE and other connective tissue diseases, rheumatoid factor and anti-cyclic citrullinated peptide for RA, viral serology including hepatitis B and C and HIV, *HLA-B27* for SpA, and *MEFV* mutations for FMF were considered.

Renal biopsy procedure

All renal biopsies were performed percutaneously by an experienced interventional radiologist under real-time ultrasonography guidance after the exclusion of renal atrophy and inequivalence in the size of both kidneys. In the absence of any contraindications, the lower left renal pole was chosen as the biopsy target, and the patient was placed in the prone position. To obtain sufficient tissue, a tru-cut biopsy two times with a 16G biopsy needle (Geotek Medical, Turkey) was performed after cleaning the skin surface area and applying local anesthesia with prilocaine. The obtained specimen was immediately sent to the pathology department and preserved on a wet sponge using saline but not formaldehyde. The patients were placed in a supine position for 4-8 hours and laid in bed for 24 hours. Monitorization of hemodynamic stability was performed with blood pressure measurement every hour and complete blood count analysis every 4 hours 3 times, in addition to evaluation of urine color for gross hematuria and pain score for hemorrhage or intraabdominal injury.

Histopathological evaluation

A sufficient amount of glomeruli was accepted as 10 or more (9-11). However, suboptimal specimens containing at least one glomerulus for each light and immunofluorescence microscopy were also examined. The histological analysis included hematoxylin and eosin, periodic acid-Schiff, Masson trichrome, and Jones methenamine silver stains for light microscopy, and a direct immunofluorescence study with IgG, IgA, IgM, C3, C1q, fibrinogen, kappa κ, and lambda λ. In all biopsies, Congo red dye was used to investigate amyloidosis. The Oxford classification (4) and International

Society of Nephrology/Renal Pathology Society classification criteria with activity and chronicity index (1) were considered standard criteria for IgA nephropathy and lupus nephritis.

Statistical analysis

Data are presented as mean ± standard deviation or median values with range for continuous variables, according to distribution, and as frequencies for qualitative variables. Statistical analyses were performed using SPSS Statistics for Windows, version 29.0 (SPSS Inc., Chicago, IL, USA).

Ethical approval and funding

The study protocol was approved by the Institutional Research Ethics Committee (Project Number 03.02.2023/244). No funding support was received for the study.

Table I - Main characteristics of the study group.

Female/Male (n, %)	38 (53.5)/33 (46.5)
Age (mean±SD)	47.9±13.8
Rheumatologic disease	
FMF	7 (9.9)
FMF + SLE	2 (2.8)
FMF + IgA vasculitis	2 (2.8)
FMF + spondyloarthropathy	1 (1.4)
IgA vasculitis	11 (15.5)
Antineutrophil cytoplasmic antibodies associated vasculitis	10 (14.1)
Systemic lupus erythematosus	18 (25.4)
SLE + AAV	1 (1.4)
Spondyloarthropathy	7 (9.9)
Rheumatoid arthritis	3 (4.2)
Sjögren's disease	4 (5.6)
Post-infectious polyarthritis and proteinuria	1 (1.4)
Seronegative pulmorenal syndrome	1 (1.4)
ANA positivity, proteinuria and elevated APR	2 (2.8)
VEXAS	1 (1.4)
Comorbidity (n, %)	
Diabetes mellitus	15 (21.1)
Hypertension	17 (23.9)
Thyroid disease	10 (14.1)
Chronic renal disease	7 (9.9)
Coronary artery disease	6 (8.5)
Congestive heart failure	2 (2.8)
Pulmonary hypertension	2 (2.8)
Interstitial lung disease	1 (1.4)
Kikuchi-Fujimato disease	1 (1.4)
Renal cell carcinoma	1 (1.4)

SD, standard error; FMF, familial Mediterrenean fever; SLE, systemic lupus erythematosus; IgA, immunoglobulin A; AAV, antineutrophil cytoplasmic antibodies-associated vasculitis; APR, acute phase reactants; ANA, anti-nuclear antibody; VEXAS, vacuoles, E1 enzyme, X-linked, autoinflmmatory, somatic syndrome.

RESULTS

Demographics of study groups

This study was conducted on 33 male and 38 female patients (46.5% *vs* 53.5%) with a median age of 47 years (range 18-78 years). Demographic and clinical features and laboratory parameters are reported in Tables I and II. Although C-reactive protein was increased in some patients, which fact was explained by disease activity, none of the patients showed increased serum procalcitonin levels before renal biopsy, suggesting a bacterial or fungal infection.

Preparation for the renal biopsy procedure

The median interval between hospitalization and renal biopsy was 5.5 days (0-19 days). The median time of the last normal value before renal biopsy was one day (0-365 days) for creatinine, 0 (0-270 days) for platelets, and (0-330 days) for the international normalized ratio (INR). The current treatment regimen before the renal biopsy was reviewed and revised, if needed (Table III). To decrease the risk of hemorrhage, antiaggregant and/or anticoagulant drugs were discontinued before biopsy for different durations, except for one patient who underwent renal biopsy under acetylsalicyclic acid. Desmopressin was given to prevent hemorrhage only in 1 patient (1.4%) with a creatinine level of 2.26 mg/dL but not under hemodialysis. Hemodialysis/ultrafiltration was applied to 4 patients before the biopsy to decrease volume overload and/or uremic toxins.

Complications, efficacy, and safety of renal biopsy

All biopsies were performed under ultrasonography guidance, and both blood pressure and complete blood count were followed for at least 24 hours if no complication was observed. No serious complication or need for surgical intervention was observed (Table IV). Infections were seen in 9 patients in the hospitalization period following renal biopsy: 1 hemodialysis catheter infection, 1 urinary tract infection, 2 COVID-19 infections, and 5 pneumonia. No re-

Table II - Laboratory parameters before renal biopsy.

Parameter	Frequency (n, %) or median value (min-max)
Creatinine (mg/dL)	1.0 (0.4-4.38)
Urea (mg/dL)	48.8 (16.0-286.0)
CRP (mg/dL)	5.0 (0.4-258.0)
Procalcitonin (ng/mL)	0.08 (0.03-0.45)
Platelets (10^9/L)	265 (126-542)
Hemoglobin (g/dL)	11.0 (6.4-15.6)
INR	1.0 (0.8-1.3)
PT (seconds)	8.9 (7.2-11.6)
aPTT (seconds)	29.0 (17.5-45.0)
Presence of proteinuria	70 (98.6)
uPCR (gr/day)	1058 (121-11868)
24 hours proteinuria	1032 (165-6100)
Range of proteinuria None 0.2-0.5 gr 0.5-3 gr >3 gr	 1 (1.4) 10 (14.1) 52 (73.2) 8 (11.3)
Presence of hematuria	44 (62.0)
Presence of anuria	None

CRP, C-reactive protein; INR, international normalized ratio; PT, prothrombin time; aPTT, activated partial thromboplastin time; uPCR, urine protein/creatinine ratio.

Table III - Medications and treatments used prior to renal biopsy.

Variable	Frequency (n%)	Cessation before biopsy (n%)	Cessation time before biopsy Median (min-max)
Acetylsalicyclic acid	9 (12.7)	8 (88.9)	4 days (1-10)
Clopidogrel	1 (1.4)	1 (100)	5 days
Warfarin	3 (4.2)	3 (100)	7 days (5-7)
NOAC	3 (4.2)	3 (100)	1 day
LMWH	12 (16.9)	12 (100)	12 hours (12 hours-6 days)
Corticosteroid	44 (62.0)	0	N/A
NSAID	6 (8.5)	3 (60)	1 day
Plasmapheresis	4 (5.6)	0	N/A
Hemodialysis	4 (5.6)	0	N/A

NOAC, novel oral anticoagulant; LMWH, low molecular weight heparin; NSAID, non-steroidal anti-inflammatory drug.

Table IV - Complications of renal biopsy.

Concomitant infections	9 (12.7)
≥1 gr decrese in Hgb in first 24 hours	8 (11.3)
Decrease in hemoglobin, gr/dL (min-max)	1.0 (1.0-1.6)
Transfusion of erythrocyte suspension	9 (12.7)
Transfusion of fresh frozen plasma	1 (1.4)
Hematuria None Microscopic Gross	 31 (43.7) 40 (56.3) 0
Performance of control USG	16 (22.5)
USG finding Normal Hematoma	 12 (75.0) 4 (25.0)
Performance of abdominal CT	3 (4.2)

Hgb, hemoglobin; USG, ultrasonography; CT, computed tomography.

nal biopsy-associated infections were identified.

Although hemorrhage impairing hemodynamic stability was not observed, control ultrasonography was performed in 16 patients because of flank pain, microscopic hematuria, or hemoglobin decrease, and only in 4 of them (5.6%) minor hematoma was found. One patient needed a transfusion of erythrocyte suspension (1.4%). The serum creatinine levels of these 4 patients were 0.77, 1.27, 1.95, and 2.48 mg/dL, and all INR, prothrombin time, and activated partial thromboplastin time levels were within normal limits. Abdominal computed tomography was performed in 3 patients after ultrasonography, and no abnormal findings were found.

Among the 9 patients who had an erythrocyte transfusion, only one showed a minor hematoma at ultrasonography, but all had low pre-biopsy hemoglobin levels ranging from 6.4 to 9.4 mg/dL.

The number of glomeruli needed for an adequate diagnosis was accepted as 10 or more: in 62 patients (87.3%), sufficient glomeruli were obtained. In one patient, no glomerulus was obtained, while in the remaining 8 patients, the number of glomeruli ranged from 2 to 9. Among 9 patients with less than 10 glomeruli, 5 obtained histological diagnoses: AA amyloidosis (1 patient), IgA vasculitis (2 patients), and lupus nephritis (2 patients). Therefore, the diagnostic success rate of the renal biopsy was 94.4%.

Histopathological evaluation and consistency of pre- and post-biopsy diagnosis

The distribution of histopathological diagnoses is shown in Table V. The major histopathological findings were cresents in 22 patients (31.0%), global sclerosis in at least 1 glomerulus in 47 patients (66.2%), immunofluorescence activity in 46 patients (64.8%), and immune-complex nephritis in 36 patients (50.7%).

Among the lupus nephritis groups (n=16), pre-biopsy creatinine was between 0.59 and 1.35 mg/dL, except for 1 patient who had a creatinine level of 1.95 mg/dL. The median activity score was 1 (0-12) and the median chronicity score was 2 (0-6). The distribution of lupus nephritis classification was: 1 class II, 1 class III, 3 class III+V, 2 class IV, 8 class V, and 1 class VI.

The consistency of pre-biopsy diagnosis and histopathological diagnosis was 80.6% in 54 of 67 biopsies after the exclusion of non-diagnostic ones. The data on discrepant patients is detailed in Table VI.

Table V - Distribution of renal biopsy proven diagnosis.

Histopathological diagnosis	Frequency (n, %)
Lupus nephritis	16 (22.5)
IgA vasculitis	14 (19.7)
Antineutrophil cytoplasmic antibodies associated vasculitis	8 (11.3)
Membranous glomerulonephritis	6 (8.5)
AA amyloidosis	6 (8.5)
Hypertensive nephrosclerosis	5 (7.0)
Normal findings	4 (5.6)
Diabetic nephropathy	3 (4.2)
Thrombotic microangiopathy and nephrosclerosis	2 (2.8)
Antiphosholipid syndrome and pre-eclampsia	1 (1.4)
Sjogren's syndrome and cryoglobulinemic vasculitis	1 (1.4)
Membranoproliferative glomerulopathy	1 (1.4)
Non-diagnostic	4 (5.6)

IgA, immunoglobulin A.

Treatment changes and repeat biopsy

Based on the renal biopsy findings, pulse corticosteroid was given in 11 patients (15.5%), cyclophosphamide in 16 (22.5%), rituximab in 1 (1.4%), intravenous immune globulins in 4 patients (5.6%), mycophenolate mofetil in 12 patients (16.9%), and aza-

Table VI - Discrepancy of pre-biopsy diagnosis and biopsy diagnosis (13 patients).

Primary rheumatologic disease	Pre-biopsy diagnosis	Histologic diagnosis
Sjogren's disease	Sjögren's disease/tubulointerstitial nephritis	Normal findings
SLE	Lupus nephritis	Normal findings
Post-infectious polyarthritis and proteinuria	Acute post-streptococcal glomerulonephritis/ lupus nephritis	Normal findings
Rheumatoid arthritis	Drug-induced lupus nephritis/membranous glomerulonephritis	Normal findings
Rheumatoid arthritis	Tubulointerstitial nephritis/IgA myeloma	Membranoproliferative glomerulopathy
Rheumatoid arthritis	Multiple myeloma renal involvement	Hypertensive nephrosclerosis
SLE	Lupus nephritis	Membranous glomerulonephritis
SLE	Lupus nephritis	Membranous glomerulonephritis
Spondyloarthropathy	AA amyloidosis/IgA nephropathy/analgesic nephropathy	Membranous glomerulonephritis
Spondyloarthropathy	AA amyloidosis/IgA nephropathy/analgesic nephropathy	Membranous glomerulonephritis
SLE	Lupus nephritis	Thrombotic microangiopathy and nephrosclerosis
Seronegative pulmonorenal syndrome	AAV/anti-GBM disease/pulmonerenal syndrome	Thrombotic microangiopathy and nephrosclerosis
Sjogren's disease	Sjogren' disease /tubulointerstitial nephritis	Lupus nephritis

IgA, immunoglobulin A; SLE, systemic lupus erythematosus; AAV, antineutrophil cytoplasmic antibodies-associated vasculitis; anti-GBM, anti-glomerular basement membrane.

thioprin in 7 patients (9.9%) before discharge. Anti-interleukin 1 treatment, anakinra or canakinumab, was added to the treatment protocol of all patients with AA amyloidosis, even though FMF disease activity was stable.

A repeat biopsy was performed in 7 patients (9.9%): 4 to obtain a diagnosis after the failure of the first renal biopsy attempt and 3 for re-staging of disease. In a patient, a total of 3 renal biopsies were performed for re-staging and showed changes in lupus nephritis from class III to IV to VI. Another patient showed changes in lupus nephritis from class IV to V, and another one from non-specific findings to AAV.

DISCUSSION AND CONCLUSIONS

Renal involvement is one of the most important causes of morbidity and mortality in the rheumatologic disease spectrum. Therefore, renal biopsy is an irreplaceable tool not only for the diagnosis of benign or malignant primary kidney disease but also for the evaluation and identification of renal involvement in rheumatologic disorders.

Performing percutaneous renal biopsy with automatic biopsy needles under real-time ultrasonography guidance decreased the rate of complications and improved the success and safety rates compared to blind biopsy (12, 13). In the literature, complications were grouped as minor or serious complications. While lumbar or abdominal pain, hematuria, and perirenal hematoma were defined as minor complications, serious complications were defined as hemorrhage requiring surgical intervention or blood transfusion, severe infection at the biopsy site, or hemodynamic instability observed as a decline in blood pressure or hemoglobin levels (14).

In the literature, the complication rate of ultrasonography-guided percutaneous renal biopsy is approximately 1-7% for serious complications and 1.5-7% for minor complications (10, 14-16). Hemorrhage is the most common objective complication but usually remains self-limited and needs no intervention, as we saw in our study (14, 15). More than 1% drop in hemoglobin level was considered significant, and with the widely used needle sizes of 16G or 18G, small hematomas were found in 1.5-17% of patients (10, 15).

Complications of native renal biopsy include from hematuria and erythrocyte transfusion need to angiographic intervention, nephrectomy, bladder obstruction, and even death (15). Life-threatening hemorrhage and those severe outcomes were decreased thanks to the introduction of ultrasonography guidance and the use of thinner biopsy needles as 16G or 18G rather than 14G (15). In our study, we found ultrasonography-proven hematoma in 4 patients (5.6%); ultrasonography was not routinely performed in all patients but in cases of signs or symptoms such as hemoglobin decrease, pain, or hematuria. Consistently, in a large meta-analysis, routine post-biopsy ultrasonography showed 17% hematoma, while symptom-based post-biopsy ultrasonography had a hematoma rate of 5%, which is similar to our results (15).

Post-biopsy erythrocyte transfusion was not only associated with the hemorrhage; similar to our cohort, even in the absence of self-limiting or severe hemorrhage, lower pre-biopsy hemoglobin levels have also been associated with increased transfusion rates (15). In 8 of 9 patients with transfusion needs, we observed as only cause lower pre-biopsy hemoglobin levels but no hematomas. Also, although 2 attempts were routinely performed to obtain sufficient glomeruli, gross hematuria, retroperitoneal hematoma, the need for surgical intervention or vascular embolization were not observed, suggesting the safety of an ultrasonography-guided automated biopsy gun performed by an experienced interventional radiologist.

An adequate number of glomeruli is an important issue, and repeating gunshots has been shown to increase the percentage of adequate biopsies from approximately 40 to 80% (17). In our cohort, we performed a trucut biopsy two times and obtained adequate glomeruli in 87.3% of the patients, but the diagnosis rate was 94.4%; this was compatible with previous studies that used ultrasonography-guided automated biopsy guns (10, 12, 13, 16).

As we revealed in our study, although the acquired specimen affects both diagnosis and classification and also prevents misdiagnosis, all materials should be evaluated even if an insufficient number of glomeruli is obtained. In 5 of our biopsies, there were fewer than 10 glomeruli, but a diagnosis was obtained. However, this possibility depends on the type of renal disease. For example, membranous nephropathy might be diagnosed even with only one glomerulus, but pathologies characterized by focal segmental distribution, such as focal segmental glomerulosclerosis, need more than 20 glomeruli (14).
In our cohort, the most common indication and diagnosis obtained was lupus nephritis, followed by IgA nephropathy. The proportion of IgA nephropathy and lupus nephritis among the disease spectrum was also found to be high in the analysis of common renal biopsy indications in previous studies at 34.7% and 16.7%, respectively (10).
As one of the most common indications for renal biopsy, lupus nephritis management is driven mainly by the findings of renal biopsy and both induction and maintenance regimens show great changes according to the classification of lupus nephritis (1, 2, 8, 18, 19). In most of the series, class IV lupus nephritis was the most common histological subtype, but we found class V lupus nephritis more frequently (2, 19). This may be due to the wider indications of renal biopsy in our cohort, covering even mild proteinuria and relatively normal serum creatinine levels at biopsy time, in contrast with previous studies that showed a more frequent presence of class IV lupus nephritis in patients with lower glomerular filtration rates (19).
A repeat renal biopsy for re-staging and examining the current status of renal involvement might be considered, especially for lupus nephritis. In one study, Morales et al. performed protocol biopsies in lupus nephritis and showed that repeat biopsies provide information regarding kidney disease progression with the increase in glomerular sclerosis, tubular atrophy, and chronicity index (8). Saleh et al. found up to 40% class and 70% treatment change in repeat renal biopsies for lupus nephritis (2). In our cohort, a few lupus nephritis patients underwent repeat biopsies and showed class changes supporting the previous data.
Finally, we observed a remarkable number of patients with discrepancies in pre-biopsy and histopathological diagnoses. This issue was not highlighted before, but we think it is an interesting finding which might direct the management of patients in a different way, especially in patients with complex findings or mimicking renal involvement of rheumatologic disorder, but showing normal histopathology or other primary renal diseases, such as diabetic nephropathy, hypertensive nephrosclerosis, or membranous glomerulonephritis. There is no previous data to explain this issue, but in our hypothesis, there could be some factors that lead to this unexpectedly higher rate of discrepant results. Firstly, the biopsy indications of our clinic seemed a little bit wider, as shown in our lupus nephritis patients, and part of the patients underwent renal biopsy for either isolated hematuria or proteinuria less than 1 g/day. Therefore, detectable renal parenchymal changes had probably not yet occurred at the time of renal biopsy. Alternatively, overlapped connective tissue diseases like SLE and Sjögren's disease or the presence of unmasked comorbidities like hypertension or diabetes affecting renal tissue earlier than the overt clinical systemic findings and incidentally found in renal biopsy with the indication of another disease, may have occurred. On the other hand, thrombotic microangiopathy (TMA) is a pathology that not only presents alone but is also associated with different diseases such as SLE, uncontrolled hypertension, pulmonorenal syndromes, infections, or the use of some drugs like calcineurin inhibitors. TMA patients showed vascular injury which was more severe than that observed in renal involvement of the primary disease; these patients were not diagnosed in advance because of more aggressive renal findings compared to silent hematologic findings, which led to the escape of TMA prediagnosis. Lastly, membranous glomerulonephritis is a common cause of severe proteinuria and nephrotic syndrome and occurs in primary or secondary forms. Among well-defined causes of secondary forms, infections, drugs, cancer, or

autoimmune diseases such as SLE, RA, urticarial vasculitis, sarcoidosis, thyroiditis, Stevens-Johnson syndrome, systemic sclerosis, or SpA were identified. The differentiation of secondary membranous glomerulonephritis from renal involvement of primary disease or primary membranous glomerulonephritis is extremely important for both diverse progression rates, prognosis, and course, as well as distinct management and therapeutical interventions, including the eradication of primary disease and the choice of disparate agents (20). We think this is an interesting finding that should be evaluated in different cohorts to better understand the reasons and factors related to patients' clinical findings and center-based differences in biopsy indications.

The limitations of our study were the relatively small sample size and retrospective design, which limited the monitoring of parameters in more detail and the prevention of data loss. In conclusion, the performance of an ultrasonography-guided percutaneous renal biopsy by an experienced operator under careful control and revision of pre-biopsy treatment, laboratory and clinical findings, and a 24-hour hospitalized follow-up seem to be a safe and successful diagnostic tool. The discrepancy between pre-biopsy diagnosis and histopathological diagnosis in a notable number of patients pointed out the crucial role of renal biopsy in rheumatology practice.

Contributions

All authors contributed equally.

Conflict of interest

The authors declare no potential conflict of interest.

Ethics approval and consent to participate

The study protocol was approved by the Institutional Research Ethics Committee (03.02.2023/244).

Availability of data and materials

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

REFERENCES

1. Weening JJ, D'Agati VD, Schwartz MM, Seshan SV, Alpers CE, Appel GB, et al. The classification of glomerulonephritis in systemic lupus erythematosus revisited. J Am Soc Nephrol. 2004; 15: 241-50.
2. Saleh M, Eltoraby EE, Tharwat S, Nassar MK. Clinical and histopathological features and short-term outcomes of lupus nephritis: a prospective study of 100 Egyptian patients. Lupus. 2020; 29: 993-1001.
3. Van Daalen EE, Wester Trejo MAC, Goceroglu A, Ferrario F, Joh K, Noël LH, et al. Developments in the histopathological classification of ANCA-associated glomerulonephritis. Clin J Am Soc Nephrol. 2020; 15: 1103-11.
4. Working Group of the International Ig ANN and the Renal Pathology Society, Cattran DC, Coppo R, Cook HT, Feehally J, Roberts ISD, et al. The Oxford classification of IgA nephropathy: rationale, clinicopathological correlations, and classification. Kidney Int. 2009; 76: 534-45.
5. Koopman JJE, Rennke HG, Leatherwood C, Speyer CB, D'Silva K, McMahon GM, et al. Renal deposits of complement factors as predictors of end-stage renal disease and death in patients with lupus nephritis. Rheumatology. 2020; 59: 3751-8.
6. Durel CA, Sinico RA, Teixeira V, Jayne D, Belenfant X, Marchand-Adam S, et al. Renal involvement in eosinophilic granulomatosis with polyangiitis (EGPA): a multicentric retrospective study of 63 biopsy-proven cases. Rheumatology. 2021; 60: 359-65.
7. Kifer N, Bulimbasic S, Sestan M, Held M, Kifer D, Srsen S, et al. Semiquantitative classification (SQC) and Oxford classifications predict poor renal outcome better than the international study of kidney disease in children (ISKDC) and Haas in patients with IgAV nephritis: a multicenter study. J Nephrol. 2023; 36: 441-9.
8. Morales E, Trujillo H, Bada T, Alonso M, Gutierrez E, Rodriguez E, et al. What is the value of repeat kidney biopsies in patients with lupus nephritis? Lupus. 2021; 30: 25-34.
9. Agarwal SK, Sethi S, Dinda AK. Basics of kidney biopsy: a nephrologist's perspective. Indian J Nephrol. 2013; 23: 243-52.
10. Xie W, Xu J, Xie Y, Lin Z, Xu X, Zhang X, et al. Adequacy and complication rates of percutaneous renal biopsy with 18- *vs* 16-gauge needles in native kidneys in Chinese individuals. BMC Nephrol. 2020; 21: 337.
11. Amann K, Haas CS. What you should know about the work-up of a renal biopsy. Nephrol Dial Transplant. 2006; 21: 1157-61.
12. Lubbers H, Mahlke R, Haake C, Lankisch PG. A new fine needle for easier, single handed, ultrasound-guided biopsies, requiring less ad-

vancing forces into solid organs. Z Gastroenterol. 1993; 31: 484-5.
13. Ahmed AM, Anees M, Riaz A, Mueed S. Percutaneous renal biopsy by automated biopsy gun. J Coll Physicians Surg Pak. 2003; 13: 263-6.
14. Whittier WL. Complications of the percutaneous kidney biopsy. Adv Chronic Kidney Dis. 2012; 19: 179-87.
15. Corapi KM, Chen JL, Balk EM, Gordon CE. Bleeding complications of native kidney biopsy: a systematic review and meta-analysis. Am J Kidney Dis. 2012; 60: 62-73.
16. Roth R, Parikh S, Makey D, Foster J, Rozenblit G, Satoskar A, et al. When size matters: diagnostic value of kidney biopsy according to the gauge of the biopsy needle. Am J Nephrol 2013; 37: 249-54.
17. Geldenhuys L, Nicholson P, Sinha N, Dini A, Doucette S, Alfaadhel T, et al. Percutaneous native renal biopsy adequacy: a successful interdepartmental quality improvement activity. Can J Kidney Health Dis. 2015; 2: 8.
18. Katsuyama E, Miyawaki Y, Sada KE, Asano Y, Hayashi K, Yamamura Y, et al. Association of explanatory histological findings and urinary protein and serum creatinine levels at renal biopsy in lupus nephritis: a cross-sectional study. BMC Nephrol. 2020; 21: 208.
19. Haridasan S, Rathi M, Sharma A, Nada R, Kumar S, Ramachandran R, et al. Outcome of biopsy-proven lupus nephritis with low glomerular filtration rate at presentation. Int J Rheum Dis. 2020; 23: 1201-9.
20. Moroni G, Ponticelli C. Secondary membranous nephropathy. A narrative review. Front Med. 2020; 7: 611317.