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A one-center experience with pediatric percutaneous renal biopsy and histopathology in Ankara, Turkey

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Abstract In this study we evaluated the indications, complications, and the spectrum of histopathological results of percutaneous renal needle biopsy (PRNB) performed in our clinic. Between June 1990 and December 2006, 679 PRNBs were performed on native kidneys of 614 children (304 boys, 310 girls) with a mean age of 10.4 years. Most frequent indications for PRNB were nephrotic syndrome (47%), hematuria, and/or proteinuria (15.9%), acute renal failure (14.6%) and complex renal manifestations (18.9%). The overall complication rate was 15.2%. The most common complications were perirenal hematoma (12.4%) and macroscopic hematuria (2.6%). The most frequent histopathological group of diseases were glomerulopathies; these were diagnosed in 376 patients (61.2%) and included membranoproliferative glomerulonephritis (11.1%), mesangial proliferation (10.7%), diffuse proliferative glomerulonephritis (7.7%), and focal segmental glomerulosclerosis (7.3%) as the most frequent. The second most frequent group of histopathology was manifestations secondary to systemic diseases; these were shown in 195 patients (31.8%). Amyloidosis (11.4%) and Henoch–Schönlein nephritis (9.9%) made the majority of this group. In conclusion, our study demonstrated that PRNB is a safe procedure with usually transient complications showing the most frequent renal diseases that cause diagnostic and therapeutic difficulties for pediatric nephrologists.

Keywords Percutaneous renal needle biopsy · Children · Indications · Complications · Histopathological results · Glomerulopathies

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Introduction

Percutaneous renal needle biopsy (PRNB) is an essential method for diagnostic and prognostic evaluation of children with kidney disease. It is a safe and practical procedure that provides important information to the pediatric nephrologist in establishing the diagnosis, evaluating the acuteness and severity of the disease, monitoring disease progression, and assessing the response to therapy [1, 2].

Although many children with renal disease can be diagnosed and treated correctly without a biopsy, there

are situations where PRNB is of value. Indications for renal biopsy in children include: persistent proteinuria and/or hematuria of unknown origin, differentiation of nephrotic syndrome and/or nephritic syndrome, rapidly progressive glomerulonephritis, and acute or chronic renal failure when the cause and extent of the disease are unknown. In patients with systemic disorders such as systemic lupus erythematosus (SLE) or Henoch–Schönlein purpura (HSP), examination of renal tissue may be necessary to document the histological type and magnitude of the renal injury which is necessary in planning management of the disease [3, 4].

In this study, we evaluated the indications, complications, and histopathological results of PRNB in our clinics in order to investigate the safety of the procedure and the spectrum of renal diseases that need PRNB and cause diagnostic and therapeutic difficulties for pediatric nephrologists.

Patients and method

Between June 1990 and December 2006, 679 PRNBs were performed on native kidneys of 614 children (304 boys, 310 girls) at the Pediatric Nephrology Department of our hospital. The follow-up period for patients was between one month and seventeen years. Their ages ranged between one month and 24 years with a mean age of 10.4 years. Patients over 18 years were observed from childhood and the procedures were repeat biopsies.

After physical examination, routine workup including complete blood count and peripheric blood smear, blood chemistry, prothrombin, partial thromboplastin and bleeding times, urinalysis, daily urinary protein excretion, creatinine clearance, and renal ultrasonography was performed on all patients before the biopsy procedures. Erythrocyte sedimentation rate, C-reactive protein, serum complement, and immunoglobulin levels, antinuclear antibody, anti-DNA, and p and c antinuclear cytoplasmic antibodies were tested when necessary. Plain abdominal radiography, intravenous pyelography, or ultrasonography were used for kidney location. After obtaining consents from parents and following premedication and local anesthesia with 1% lidocaine PRNBs were performed on either the right or left kidney of patients. Until 2001 modified Vim–Silverman needles were used to obtain biopsies from patients; after this date Trucut needles were used.

Following the biopsy procedure, patients were instructed to remain in bed with a sandbag at back for 24 h. Vital signs were measured at a quarter-minute intervals for the first 2 h and hourly for a day thereafter. Each urine sample voided was examined for gross hematuria for a day. Follow-up hemoglobin measurements were performed 2–4 and 6–12 h after biopsy. Ultrasound examination of the punctured kidney has been performed in all patients on the next day and the patients were discharged after 24 h if there was no complication. Patients who developed macroscopic hematuria were followed up until the bleeding stopped. Patients with perirenal hematomas were discharged after having shown there was no progression in the size of hematomas within a few days and ultrasonography has been repeated at a two-week interval in outpatient clinics until hematomas resolved.

All biopsy specimens were studied by light microscopy and immunofluorescence microscopy at the Pathology Department of our hospital. Electron microscopic studies were performed on 46 patients who were expected to have diseases that could not be revealed by light microscopy, for example defects of the glomerular basal membrane and were evaluated in the Pathology Department of a University Hospital. This could not be performed in all patients as a routine examination, due to cost reasons. Biopsy material containing at least ten glomeruli has been considered as adequate for proper diagnosis.

Patients with an inadequate number of glomeruli underwent rebiopsies. Repeat biopsies were also performed on patients with chronic glomerulopathies in order to evaluate the stage of the disease and determine the management. A single PRNB was performed on 557 patients, two biopsies on 50, three biopsies on six patients, and four on one patient.

Biopsy indications and biopsy complications of all the patients were obtained by review of hospital records and results were given for 679 biopsy procedures. Histopathological findings were documented in percentages for 614 patients, after repeat biopsies were excluded, in order to demonstrate the frequency of renal diseases.

Results

In a period of 16.5 years 679 PRNBs were performed. During the procedure, edema was present in

335 patients, hypertension in 130, and rash in 98 patients (Table 1). Laboratory examinations revealed hematuria in 310 patients (164 microscopic, 146 macroscopic), proteinuria in 497 (369 in nephrotic range), hypoalbuminemia in 395, deteriorated renal functions in 198, and anemia in 144. Blood urea nitrogen levels were between 2 and 210 mg/dl (mean 33.6 mg/dl), serum creatinine levels 0.1–17 mg/dl (mean 1.59 mg/dl), and albumin 0.6–5.5 g/l (mean 2.8 g/dl).

Most frequent indication for PRNB was nephrotic syndrome which was found in 319 patients (47.0%) (Table 2). Hematuria and/or proteinuria was the indication in 108 patients (15.9%), acute renal failure in 99 (14.6%), chronic renal failure in 22 (3.2%), and complex renal manifestations in 128 (18.9%). Three patients with SLE without any renal findings underwent PRNB for classification.

The overall complication rate was 15.2%. The most common complication was perirenal hematoma that was seen in 84 patients (12.4%) (Table 3). Only two patients needed blood transfusion and all of these resolved spontaneously within 2–8 weeks. Macroscopic hematuria developed in 18 patients (2.6%) who had no gross hematuria previous to PRNB. In one patient with chronic renal failure an arteriovenous fistula developed with accentuation of his hypertension. With continuous ambulatory peritoneal dialysis and antihypertensive treatment his blood pressure was controlled and he did not need any surgical treatment.

Table 1 Spectrum of clinical and laboratory findings of patients during the biopsy procedure

Clinical or laboratory finding	Number of patients (%)
Edema	335 (49.3)
Hypertension	130 (19.1)
Rash	98 (14.4)
Hematuria	310 (45.6)
Microscopic	164 (24.1)
Macroscopic	146 (21.5)
Proteinuria	497 (73.2)
Non-nephrotic range	128 (18.9)
Nephrotic range	369 (54.3)
Hypoalbuminemia	395 (58.2)
Deteriorated renal functions	198 (29.2)
Anemia	144 (21.2)

Table 2 Indications for renal biopsy

Indication	Number of patients (%)
Nephrotic syndrome	319 (47.0)
Hematuria and/or proteinuria	108 (15.9)
Acute renal failure	99 (14.6)
Chronic renal failure	22 (3.2)
Complex renal manifestations	128 (18.9)
Normal renal findings*	3 (0.4)

* Patients with SLE for classification

Biopsy specimens included 0–139 glomeruli. In 34 patients the number of glomeruli was inadequate for exact diagnosis and adequate specimens were obtained from all of these patients by rebiopsies. The success rate of PRNB was 95.0%.

The most frequent histopathological group of diseases were glomerulopathies; these were diagnosed in 376 (61.2%) patients (Table 4). The most frequent glomerulopathy detected by PRNB was membranoproliferative glomerulonephritis (MPGN), which was shown in 68 patients (11.1%). This was followed by mesangial proliferation (10.7%), diffuse proliferative glomerulonephritis (7.7%), focal segmental glomerulosclerosis (FSGS) (7.3%), chronic glomerulonephritis (5.7%), minimal change disease (MCD) (5.4%), idiopathic crescentic glomerulonephritis (3.6%), membranous glomerulonephritis (3.4%), IgA nephropathy (3.4%), IgM nephropathy (2.3%), Finnish type nephrotic syndrome (0.3%), and diffuse mesangial sclerosis (0.3%). Apart from 22 patients with idiopathic crescentic glomerulonephritis, 34 more patients had crescentic glomerulonephritis associated with other renal diseases including HSP (20), MPGN (6), diffuse

Table 3 Complications of PRNB

Complication	Number of patients (%)
Transient complications*	102 (15.0)
Perirenal hematoma	84 (12.4)
Macroscopic hematuria	18 (2.6)
Permanent complications	1 (0.1)
Arteriovenous fistula**	1 (0.1)
Total	103 (15.2)

* All resolved spontaneously

** This patient had chronic glomerulonephritis with renal failure and hypertension at presentation. He is now on a CAPD program and his blood pressure is under control

Table 4 Histopathological findings for 614 patients

Histopathological finding	Number of patients (%)
Glomerular diseases	**376 (61.2)**
Membranoproliferative glomerulonephritis	68 (11.1)
Mesangial proliferation	66 (10.7)
Diffuse proliferative glomerulonephritis	47 (7.7)
Focal segmental glomerulosclerosis	45 (7.3)
Chronic glomerulonephritis	35 (5.7)
Minimal change disease	33 (5.4)
Idiopathic crescentic glomerulonephritis	22 (3.6)
Membranous glomerulonephritis	21 (3.4)
IgA nephropathy	21 (3.4)
IgM nephropathy	14 (2.3)
Finnish type nephrotic syndrome	2 (0.3)
Diffuse mesangial sclerosis	2 (0.3)
Systemic diseases	**195 (31.8)**
Amyloidosis	70 (11.4)
Henoch–Schönlein purpura	61 (9.9)
Systemic lupus erythematosus	46 (7.5)
Poliarteritis nodosa	12 (2.0)
Hemolytic uremic syndrome	5 (0.8)
Wegener granulomatosus	1 (0.2)
Hereditary and congenital diseases	**14 (2.3)**
Cystic kidney diseases	6 (1.0)
Alport syndrome	5 (0.8)
Thin membrane disease	3 (0.5)
*Tubulointerstitial nephritis***	**14 (2.3)**
Miscellaneous	**15 (2.4)**
Oxalosis	7 (1.1)
Chronic pyelonephritis	3 (0.5)
Toxic nephropathy	1 (0.2)
Renal infarct	1 (0.2)
Lymphoma	1 (0.2)
Nephrocalcinosis	1 (0.2)
Nephronophtisis	1 (0.2)

Main groups of diseases are shown in bold, subgroups with normal characters

*Secondary crescentic glomerulonephritis was also found in 34 other patients and was associated with their primary renal pathologies including HSP (20), MPGN (6), diffuse proliferative glomerulonephritis (4), IgAN (2), HUS (1) and SLE (1), and they were categorized in their primary pathologies

**Tubulointerstitial nephritis was also found in 21 other patients in which it was associated with other renal diseases and categorized in their primary pathologies

proliferative glomerulonephritis (4), IgAN (2), HUS (1) and SLE (1); these were categorized in their primary pathologies.

The second frequent group of histopathology was manifestations secondary to systemic diseases that was shown in 195 (31.8%) patients. Amyloidosis secondary to familial Mediterranean fever (FMF) (11.4%) and Henoch–Schönlein nephritis (9.9%) formed the majority of this group. SLE was diagnosed in 46 patients (7.5%) and in most of these PRNB was performed for classification. Twelve patients (2.0%) were found to have poliarteritis nodosa (PAN), five hemolytic uremic syndrome (HUS), and one Wegener granulomatosus (WG). Tubulointerstitial nephritis (TIN) was found in 35 patients. This was the sole histopathological finding in 14 patients; in 21 others it was found to accompany another renal pathology. These 21 patients with TIN associated with other histopathological findings were also categorized in their primary pathologies.

Fourteen patients had hereditary and congenital diseases including cystic renal diseases (six patients),

Table 5 Patients with repeat biopsies

Histopathological finding in first PRNB	Number of patients with two biopsies	Number of patients with three biopsies	Number of patients with four biopsies
MPGN	8	3	–
SLE	5	–	–
FSGS	3	1	–
MGN	–	2	1
Inadequate material	34	–	–
Total	50	6	1

PRNB: percutaneous renal needle biopsy; MPGN: membranoproliferative glomerulonephritis; SLE: systemic lupus erythematosus; FSGS: focal segmental glomerulosclerosis; MGN: membranous glomerulonephritis

Alport syndrome (five patients), and thin membrane disease (three patients). Cystic renal diseases included cystic renal dysplasia in two patients and polycystic kidney disease in four. Seven patients had oxalosis, three had chronic pyelonephritis, and one each had cyclosporine-A toxicity, renal infarct, lymphoma, nephrocalcinosis, and nephronophtisis.

As shown in Table 5, 50 patients underwent a second PRNB while six patients had three and one had four biopsies. Of the patients that had two biopsies, 34 patients underwent another biopsy because of inadequate biopsy material, so appropriate tissue could be obtained. Eleven patients with MPGN, five with SLE, four with FSGS, and three with MGN also had repeat biopsies to determine the stage of the disease and/or for planning management of the disease.

Discussion

Since the introduction of PRNB in 1934 by Ball, it has been widely used throughout the world, especially since the 1950s, for diagnostic and prognostic evaluation of various nephropathies [4–6]. It has also been accepted as a safe and practical procedure in children. However, there is also a risk of several complications such as gross hematuria, perirenal hematoma, arteriovenous fistulas, infection, damage to adjacent organs, or loss of the kidney [7–15]. The complications and their rates must therefore be well known and the decision to perform PRNB must be made if the clinical benefit overcomes the risk of the procedure. In this study, we investigated the frequency of complications of PRNB in children followed up in our center and documented the indications and histopathological results in order to find the range of diseases for which the children underwent this procedure.

We performed 679 biopsies on 614 children with a success rate of 95% and an overall complication rate of 15.2%. All complications except one were transient, including perirenal hematoma and macroscopic hematuria and resolved spontaneously. The rate at which an adequate amount of tissue is yielded by PRNB in children usually varies between 92% and 98.7% [1, 8, 16–18]. According to the different centers and technical equipment it may range from 69% to 100% [1, 19]. The overall complication rates in different series were between 11.4% and 22% although it may be as low as 2.6% and as high as 43% [1, 2, 8, 16–20]. In our series the success rate and frequency of complications were no different from those of most of the studies performed on children although the latter seemed to be higher than many studies. The most frequent complication in our study was perirenal hematoma (12.4%); this was diagnosed by routine ultrasonographic examinations performed on the following day of the procedure, although most of the patients were symptom free. Our relatively high complication rate may be because this routine screening of complications was not used in many of the studies reported in the literature.

In the literature nephrotic syndrome is the most common indication for renal biopsy both in children and in adult patients, accounting for approximately 42–47% of patients [21–23]. In our study the most frequent indication for PRNB was also nephrotic syndrome (47%) which was followed by urinary abnormalities, for example hematuria and/or proteinuria (15.9%) and acute renal failure (14.6%). Complex renal manifestations including more than

one of the above findings were the indication for PRNB in 18.9% of patients. Three patients with SLE underwent PRNB for classification although they did not have any renal findings, because it is the protocol of our clinics for SLE patients.

There are relatively few studies demonstrating the histopathological findings of renal biopsies in the literature and they usually include all age groups. The most frequent histopathological group of diseases found in all studies is primary glomerulonephritis in both children and adult patients [21–26]. IgA nephropathy is the most frequent glomerulopathy in adults whereas MPGN and FSGS are the most common in children [22–26]. In our study the most frequent histopathological findings were also glomerular diseases (61.2%), as expected; MPGN, mesangial proliferation, diffuse proliferative glomerulonephritis, and FSGS are the most common glomerulopathies that we found. All 22 patients with idiopathic crescentic glomerulonephritis were idiopathic and pauciimmune. With the additional 34 patients associated with other renal diseases, crescentic glomerulonephritis seemed to be high in our series which might probably be explained by genetic predisposition in our country .

The second most frequent group of histopathology was renal pathologies secondary to systemic diseases, which were shown in 195 patients. The most striking feature in our study is that amyloidosis secondary to FMF was found in 70 patients which makes 11.4% of all study group and which does not exceed 0.5–3% in the literature [22, 23, 25]. Henoch–Schönlein nephritis and SLE are the other diseases which make the majority of this group. Twelve patients were found to have PAN, five HUS, and one WG.

In conclusion, PRNB in children is a safe procedure with usually transient complications that resolve spontaneously and a low rate of permanent complications. It is an important procedure that enables identification of several renal pathologies, especially glomerular and systemic diseases that need immediate and appropriate management. Our study revealed the most frequent renal diseases that cause diagnostic and therapeutic difficulties for pediatric nephrologists which have rarely been reported in the literature, especially for children. The finding in our study most different from literature reports was the high percentage of amyloidosis, reflecting its frequency in our country.

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