Nephrectomy for Non-neoplastic Kidney Diseases

Joseph P. Gaut, MD, PhD

KEYWORDS

• Chronic pyelonephritis • Dysplasia • ADPKD • ARPKD • Xanthogranulomatous pyelonephritis • Reflux nephropathy • Obstructive nephropathy

ABSTRACT

This review discusses the pathology of non-neoplastic kidney disease that pathologists may encounter as nephrectomy specimens. The spectrum of pediatric disease is emphasized. Histopathologic assessment of non-neoplastic nephrectomy specimens must be interpreted in the clinical context for accurate diagnosis. Although molecular pathology is not the primary focus of this review, the genetics underlying several of these diseases are also touched on.

OVERVIEW

Nephrectomy is the mainstay of treatment of non-neoplastic renal diseases of various causes. A search of the pathology archives of the Barnes Hospital Lauren V. Ackerman Laboratory of Surgical Pathology revealed a majority, 175 of 295 (59%), of partial or total nephrectomies in the pediatric (<18 years) population were performed for non-neoplastic causes. The most common pathologic diagnoses in such cases were obstructive nephropathy, renal dysplasia, and chronic pyelonephritis (**Table 1**). Reflux nephropathy was frequently diagnosed in combination with renal dysplasia and/or obstruction. Trauma, autosomal recessive polycystic kidney disease (ARPKD), congenital nephrotic syndrome with intractable proteinuria, venous thrombosis, severe oxalosis, lithiasis, renal hypoplasia, and agenesis were also identified as diagnoses rendered in pediatric nephrectomies but were considerably less common. Of the patients with chronic pyelonephritis, vesicoureteric reflux (VUR) and obstruction were the most common associated causes. A summary of the major causes and the key diagnostic features is outlined in **Table 2**. Previous studies showed a similarly high incidence of non-neoplastic entities among pediatric nephrectomy specimens.[1,2] Several of these entities may coexist. For example, patients with reflux nephropathy may also have chronic pyelonephritis.

CHRONIC PYELONEPHRITIS

Chronic pyelonephritis as a descriptive term refers to the presence of chronic tubulointerstitial inflammation and scarring secondary to bacterial infection; it can be associated with urine reflux from the lower urinary tract or urine flow obstruction. A precise diagnosis requires clinical and radiographic correlation and involvement of the renal pelvis by inflammation. It may be broken into obstructive and nonobstructive pyelonephritis. Urine reflux is most commonly due to an incompetent ureterovesical valve located at the entry of the ureter into the bladder, known as the *ureterovesical junction*, and is referred to as VUR. VUR is the underlying cause of disease in many children with chronic nonobstructive pyelonephritis. The term, *reflux nephropathy*, was introduced and is distinguished from pyelonephritis by the presence of discrete scars in a lobar distribution. Because reflux nephropathy does not require history of bacterial infection, it may be used in cases of sterile reflux. Similarly, the term, *obstructive nephropathy*, is used when a definitive cause of obstruction, either functional or structural, can be identified. The terms, *reflux nephropathy* and *obstructive nephropathy*, have caused considerable confusion

Nephropathology Associates, 10810 Executive Center Drive, Suite 100, Little Rock, AR 72211, USA
E-mail address: joe.gaut@nephropath.com

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Table 1
Review of pathology case records from the Barnes Hospital Lauren V. Ackerman Laboratory of Surgical Pathology

Cause	Number of Cases
Non-neoplastic	175 (59%)
Obstruction ± reflux ± chronic pyelonephritis	63 (36%)
Dysplasia ± reflux ± obstruction	58 (33%)
Chronic pyelonephritis	19 (11%)
Trauma	12 (7%)
Reflux nephropathy	7 (4%)
Congenital nephrotic syndrome	3 (2%)
Venous thrombosis	2 (1%)
ARPKD	1 (<1%)
Oxalosis	1 (<1%)
Hypoplasia	1 (<1%)
Agenesis	1 (<1%)
Lithiasis	1 (<1%)
ESRD, unknown	6 (3%)
Neoplastic	120 (41%)
Wilms tumor	76 (63%)
Other	44 (37%)

Case records were reviewed between 1989 and 2013. Patients under the age of 18 who underwent partial or total nephrectomy were included. A total of 295 nontransplant cases were identified.

but a good rule for applying the term, *chronic pyelonephritis*, is history of recurrent urinary tract infections (UTIs) irrespective of the presence or absence of VUR and/or obstruction.

GROSS FEATURES OF CHRONIC PYELONEPHRITIS

Grossly, kidneys with chronic pyelonephritis are small with irregular parenchymal scarring. The number and location of scars vary, but the renal poles tend to be preferentially involved. The cortical surface may be smooth, particularly in cases of congenital VUR, or granular when associated with arterionephrosclerosis. Hydronephrosis (dilatation of the pelvis and or calyces) is present to varying degrees. In general, cases associated with obstruction show more severe hydronephrosis (**Fig. 1**A). Cystic changes are frequent and the cortex is thinned (atrophic). There are no specific gross findings to distinguish infectious from noninfectious renal cortical scarring.

MICROSCOPIC FEATURES

Histologic examination of nephrectomy specimens from patients with chronic pyelonephritis demonstrates scarring that is most prominent at the renal poles. The tubules are atrophic and have a thyroidization appearance, named for the superficial resemblance to normal thyroid parenchyma (see **Fig. 1**B). Thyroidization is not a pathognomonic finding of past infections but is commonly associated with chronic parenchymal damage of all causes. A patchy chronic inflammatory infiltrate is present within the interstitium of the cortex, the medulla, or both the cortex and medulla. The inflammatory cells are a mixture of lymphocytes, monocytes, and plasma cells. The inflammatory infiltrate may be dense and show germinal center formation (see **Fig. 1**C). If there is a neutrophilic predominant infiltrate with neutrophilic tubular casts, a superimposed acute infection should be

Table 2
Key pathologic features

Diagnosis	Histologic and Associated Findings
ARPKD	Columnar-shaped cysts
ADPKD	Spherical cysts with flat, cuboidal, or papillary lining
Dysplasia	Immature tubules with fibromuscular collars
Congenital VUR	Renal scarring with segmental renal dysplasia; clinical history of reflux
Acquired VUR	Renal scarring without dysplasia; clinical history of reflux
Chronic pyelonephritis	Renal scarring with tubule thyroidization and pelvic inflammation associated with infection
Obstructive nephropathy	Interstitial fibrosis/tubular atrophy associated with functional or mechanical obstruction
XGP	Renal scarring associated with infection. Numerous foamy histiocytes. May mimic tumor
NPHP-MCKD	Corticomedullary cysts, tubular disruption, tubular atrophy