Renal Biopsy and Pathology

Alexander Kats, MD
Pediatric and Renal Pathology

The function of the nephropathology group of the Children’s Mercy Hospital is an ultimate teamwork exercise, involving nephrologists, pathologists, and highly skilled laboratory technologists, allowing optimal clinicopathological correlations and diagnoses which give specific categorization of renal disease, etiologic and prognostic information.

Renal needle biopsy is considered a gold standard in morphologic evaluation of multiple kidney diseases. Historically, histopathologic evaluation of kidney diseases was based on the autopsy material. The first renal biopsy was performed in the beginning of the century [1]; however, systematic performance and histologic evaluation of renal biopsies gained widespread introduction into clinical use in the 1950s, after Castleman’s and Smithwick’s research [2]. Later, Heptinstall examined large series of open renal biopsies taken at the time of dorsolumbar sympathectomy, a procedure used to treat hypertension [3]. Evaluation of those biopsies provided first insight into vascular pathology associated with hypertension and established reliability of the biopsy material by comparing samples taken from both kidneys. The publication of the results of 133 aspiration kidney biopsies in 1951 led to an increased interest in diagnostic renal biopsies [4].

The introduction of a spring-loaded biopsy gun in the last 25 years, combined with newer visualization methods, such as ultrasound guidance and computed axial tomography scanning, has led to greater tissue yield of the biopsy material and a much lower risk of complications. After the CIBA Symposium on Renal Biopsy, Clinical and Pathological Significance held in London, England, in March of 1961, renal biopsy became a key part of renal evaluation. Overall, renal biopsy has played a critical role in the development of nephrology as a subspecialty.

An ultrasound scan is used to localize an optimal biopsy site. The lower pole of the native left kidney and the most visible or easily accessible pole of the transplant kidney are the usual biopsy sites. Following local anesthesia, the skin is incised, and the biopsy needle is inserted. Using real-time ultrasound guidance, the needle is advanced to the kidney, and the biopsy gun is triggered. The number of biopsy attempts varies. Usually two or three attempts with 14 or 18 gauge needle produce a desired result. A pathologist, nephrologist, or trained technologist quickly determines the adequacy of the sample using a dissection microscope. Most renal biopsies can be done percutaneously; however, a transjugular retrograde approach or laparoscopic technique can be also utilized.

For an accurate diagnosis, renal biopsy is evaluated with light microscopy, immunohistochemistry, and transmission electron microscopy (EM). The biopsy material is triaged using a dissection microscope and placed into appropriate media for all three diagnostic modalities. Rapid tissue fixation with minimal delay from the time of biopsy to the entry into fixative is required for quality light microscopy and EM morphology.

Light microscopy: Multiple serial sections at 2 to 3 µm are critical for accurate evaluation of the renal biopsy material. Different alternating stains, such as hematoxylin-eosin, periodic acid–Schiff, Jones silver, and Trichrome, are used on the multiple level sections for combined evaluation of normal kidney structures and pathologic lesions.

Immunofluorescence microscopy: A portion of a sample for immunofluorescence microscopy is usually quickly frozen or immersed in special transport media. A routine diagnostic kidney biopsy should be examined for the presence of immunoglobulin deposits (IgG, IgM, and IgA), complement components (C3, C1q, C4), fibrin, and, in some instances, kappa and lambda light chains. Some of the medical conditions require more specialized studies,
such as alpha chains of collagen-type IV in hereditary nephritis or C4d in renal transplant biopsies. Our laboratory has recently implemented and validated a C4d immunohistochemical stain to utilize on the formalin-fixed and paraffin embedded renal allograft biopsies, to complement immunofluorescence method (Picture 1). Viral stains, such as SV-40, a surrogate immunohistochemical marker of polyoma virus infection (BK-Virus) and CMV, are also utilized.

Electron microscopy: Tissue for transmission EM is processed and embedded into plastic (epoxy). 1-µm “thick” sections are cut and stained with toluidine blue. Evaluation of these sections under light microscopy helps to determine presence of the glomeruli and other structures and select the areas for ultrastructural evaluation. In addition, histopathologic lesions, such as FSGS, arterial emboli and/or granular intracellular cytoplasmic inclusions in Fabry’s disease can be found under light microscopy. The ultra thin sections are cut and collected on copper grids. These sections are stained with heavy metal salts and then examined under electron microscopy. Multiple microphotographs are taken at different magnifications. The glomerular capillary loops and mesangium of the “native” kidney biopsy are evaluated for presence and localization of the immune-type electron dense deposits, structural abnormalities of the glomerular basement membrane, epithelial and endothelial cells components, and pathologic inclusions within the cellular components.

Renal biopsy interpretation and report include a detailed description of the findings, present on a variety of light microscopy stains, immunohistochemistry materials, and EM photomicrographs. All renal compartments, such as glomeruli, tubulointerstitium, and vessels are described in a systematic manner. These findings are correlated with detailed clinical information and, possibly, with the previous biopsy material, allowing thorough understanding of the disease process and providing prognosis in many instances.

Renal transplant biopsy is a gold standard for the diagnosis of the episodes of graft dysfunction that occur in 30-60% of patients after transplantation and helps to distinguish acute rejection from acute tubular injury, calcineurin inhibitor toxicity, or chronic rejection. Allograft biopsy also helps to identify concurrent “de novo” or recurrent primary disease. Renal biopsy has changed the clinical diagnosis in 27-46% of the cases and therapy in 59% of the reported series, with no obvious diminishing value in the last 20 years. Most importantly, renal biopsy findings have lead to reduced immunosuppression in 22% of the patients [5]. Two cores from the allograft biopsy are preferred and divided for light and immunofluorescence microscopy. The small portion could be processed for electron microscopy, if glomerular disease is suspected. Two cores increase diagnostic sensitivity of rejection up to 99% [6]. The “protocol” renal allograft biopsies reveal significant percentage of subclinical rejection at every examined time point [7]. The finding of subclinical rejection has been associated with decreased graft survival at 10 years, and there is evidence that treatment of subclinical rejection improves long-term results [8].
It is thought that advances in the multiple new analytical methods, such as molecular pathology, using CGH arrays and proteomics, may result in a decrease in use of renal biopsy for diagnosis of kidney diseases. However, a complex structure of the nephron and supporting elements, as well as difficulties in identifying specific molecular pathways within the whole organ fragments, present an ongoing challenge for renal pathology. The classic evaluation of the kidney morphology combined with emerging new analytical methods will provide a better insight into the pathologic processes of multiple renal diseases and lead to more specific diagnoses and treatment options.