Renal Biopsy and Pathologic Evaluation of Glomerular Disease

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Presence of suspected primary glomerular disease is the most common and compelling reason to consider renal biopsy. Pathologic findings in samples from animals with nephritic or nephrotic glomerulopathies, as well as from animals with persistent subclinical glomerular proteinuria that is not associated with advanced chronic kidney disease, frequently guide treatment decisions and inform prognosis when suitable specimens are obtained and examined appropriately. Ultrasound-guided needle biopsy techniques generally are satisfactory; however, other methods of locating or approaching the kidney, such as manual palpation (e.g., in cats), laparoscopy, or open surgery, also can be used. Visual assessment of the tissue content of needle biopsy samples to verify that they are renal cortex (i.e., contain glomeruli) as they are obtained is a key step that minimizes the submission of uninformative samples for examination. Adequate planning for a renal biopsy also requires prior procurement of the fixatives and preservatives needed to process and submit samples that will be suitable for electron microscopic examination and immunostaining, as well as for light microscopic evaluation. Finally, to be optimally informative, renal biopsy specimens must be processed by laboratories that routinely perform the required specialized examinations and then be evaluated by experienced veterinary nephropathologists. The pathologic findings must be carefully integrated with one another and with information derived from the clinical investigation of the patient's illness to formulate the correct diagnosis and most informative guidance for therapeutic management of the animal's glomerular disease.

Keywords: kidney, glomerular disease, renal biopsy, renal pathology, dog, cat, proteinuria

The purpose of renal biopsy is to obtain information that can help the clinician manage a patient's illness more astutely than might be possible without the biopsy and thus to obtain the best available outcome. This information might be the diagnosis of a particular nephropathic illness for which specific therapeutic options can be defined or refined. Additionally, and often independent of identifying a specific etiopathogenic diagnosis, renal biopsy typically yields information about the likely mechanism(s) of injury, as well as the severity, activity, chronicity, and/or potential reversibility of pathologic changes that are present, all of which support clinical decision-making about prognosis and treatment.[1-5]

To achieve this purpose, 3 things must be true. First, the biopsy must be indicated; that is, it must be performed in a clinical situation in which the results of the biopsy will have potential utility. Second, the biopsy procedure itself (i.e., the process of obtaining adequate kidney tissue samples) must be done safely. Third, the tissue samples must be evaluated by individuals having expertise in nephropathology and using all the methods required to adequately characterize the important pathologic changes in the specimens and thus yield the most informative diagnosis. For suspected glomerular disease, which is the focus of this article, the required methods of evaluation are highly specialized and include special sectioning and staining protocols for the light microscopic evaluation, as well as routine use of transmission electron microscopic and immunostaining evaluations.

Indications

The presence of suspected glomerular disease is the most common and compelling reason to consider performing renal biopsy. Because proteinuria is a hallmark of glomerular injury, this particular laboratory test abnormality often is a key factor that prompts consideration of a renal biopsy. However, proteinuria has many possible causes and proteinuria in and of itself is not an appropriate indication for renal biopsy. The key point here is that it actually is the identification of a

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proteinuric nephropathy (i.e., renal disease characterized a least in part by proteinuria) rather than the proteinuria per se that should prompt consideration of renal biopsy. A discussion of the proper assessment of proteinuria is beyond the scope of this article, but appropriate guidance is available elsewhere.[6]

Animals with proteinuric nephropathies for which renal biopsy should be considered usually are those that exhibit a nephritic or nephrotic glomerulopathy or have glomerular disease that is characterized by persistent subclinical renal proteinuria.[4,5] Many animals, especially dogs, with chronic kidney disease that has advanced to International Renal Interest Society stage IV or late stage III exhibit some proteinuria; however, biopsy of these animals usually is unrewarding and generally should be avoided.

Nephritic glomerulopathies are characterized by proteinuria that can have a wide range of magnitude but often is in the nephrotic range (arbitrarily defined as UPC > 3.5), with or without accompanying hypoalbuminemia that usually is of mild to moderate severity when it is present, and urinalysis findings that include signs of inflammation in the urinary tract (e.g., microscopic hematuria, mild pyuria). Most animals with nephritic glomerulopathies exhibit azotemia (the magnitude of which can be mild to severe) that typically also shows a rising trend in acute cases. Additionally, hypertension that frequently is severe and difficult to control medically often is present; however, edema or ascites is uncommon.

Animals with nephrotic glomerulopathies exhibit nephrotic range proteinuria associated with marked hypoalbuminemia that may or may not be associated with evident edema or third-space accumulation of transudates (e.g., ascites, pleural effusion). Animals with nephrotic glomerular diseases usually have totally inactive urine sediments and often do not have azotemia, especially early in the disease course. Hypertension is a variable feature of nephrotic glomerulopathies.

Animals with persistent subclinical renal proteinuria (proteinuria that is not of prerenal or postrenal origin and has been repeatedly documented over a period of a month or more in an animal that exhibits no related clinical signs) may have proteinuria of any magnitude, but it usually is of mild to moderate severity and associated with normal or only mildly decreased circulating albumin concentrations. These animals may or may not be azotemic. Indeed, this category overlaps with chronic kidney disease, especially in International Renal Interest Society stages I and II, and early stage III. These are among the most challenging animals in which to decide whether a biopsy will be useful. In general, the higher the UPC and the lower (i.e., more normal or near-normal) the serum creatinine concentration, the more a recommendation to biopsy can be supported, but each case should be considered individually instead of by applying any single UPC or serum creatinine cut off. In borderline cases, however, it is logical to be swayed toward biopsy by finding lack of response or worsening trends during treatment with nonspecific renoprotective interventions (i.e., feeding an appropriate diet, administering drugs to block portions of the renin-angiotensin-aldosterone system, etc.).

Figure 1. A mobile cart used at Texas A&M University to aid in the processing of renal biopsy specimens. The cart is readily taken to whatever site in the hospital (e.g., surgery or ultrasound suite, etc.) where specimen collection is planned. The top of the cart is prepared for processing a biopsy on-site. Note the dissecting microscope, which is used to assess specimen content. There also is an ice bucket to keep the fixative for electron microscopy chilled, as well as a thermos containing liquid nitrogen used to snap freeze samples for immunofluorescence microscopy after a shallow puddle of the liquid nitrogen is poured into the styrofoam freezing box.

Contraindications

Regardless of the indications for renal biopsy, it should not be performed (or should at least be delayed until the patient's condition is stabilized) if it cannot be performed safely. The main renal biopsy complication of clinical concern is serious hemorrhage.[7,8] Factors that are associated with increased risk of this complication are small patient size (i.e., small size of the biopsy target relative to adjacent large vessels), especially animals that weigh less than 5 kg, as well as the presence of disordered hemostasis (e.g., thrombocytopenia, prolonged bleeding time, etc.) or uncontrolled hypertension. Other relative or absolute contraindications to renal biopsy include inadequate control of patient pain or motion (including breathing), and insufficient operator competence.

Prebiopsy Planning

Adequate planning for a renal biopsy requires prior procurement of the materials needed to process and submit samples that will be suitable for the required examinations (Fig 1).