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Review Article

Biopsy in native kidney diseases

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ABSTRACT

Renal biopsy is usually obtained to establish a diagnosis, help guide therapy, and ascertain the degree of active and chronic changes. The routine evaluation of a percutaneous renal biopsy involves examination of the tissue under light, immunofluorescence, and electron microscopy. The indications for performing a renal biopsy vary among concerned physicians, being determined in part by the clinical features, signs, and symptoms. Among patients with the nephrotic syndrome and no evidence of systemic disease, renal biopsy is performed both to determine treatment and to make an unidentified diagnosis. The acute nephritic syndrome is often caused by a systemic disease that requires a renal biopsy to establish the diagnosis and guide treatment. Even in the absence of a systemic disease, the acute nephritic syndrome commonly needs a biopsy to ascertain a diagnosis and guide treatment. Among patients with unexplained acute kidney injury, a biopsy is obtained in those settings, in which the diagnosis is uncertain. Among patients with isolated glomerular hematuria, a renal biopsy is not routinely performed, unless there is evidence of progressive disease such as increasing proteinuria or a rising serum creatinine concentration. A renal biopsy is also generally not obtained in patients, who presents with low-grade proteinuria (less than 500–1000 mg/day), the absence of glomerular hematuria, usually normal renal function, and an absence of clinical or serologic evidence of a systemic disease that can cause glomerulonephritis. Prior to a percutaneous renal biopsy, a history, physical examination, and selected laboratory tests should be performed. Recommended laboratory tests include complete blood count, platelet count, prothrombin time, partial thromboplastin time, and bleeding time. Percutaneous renal biopsy is usually performed under real time ultrasonic guidance in local anesthesia with spring-loaded needle. Bleeding is the primary complication of renal biopsy. Nonpercutaneous renal biopsies (open, laparoscopic, and transjugular renal biopsy) are indicated in settings, in which a percutaneous renal biopsy cannot be performed (uncorrectable bleeding diathesis, failed attempts at percutaneous biopsy).

1. Introduction

A percutaneous renal biopsy is usually obtained for various reasons, like for establishment of an diagnosis, as an aid to know nature of prescribed therapy or to decide, when treatment is futile, and to ascertain activity (i.e., potentially reversible) and chronicity (i.e., irreversible).[1,2] The degree of activity or chronicity on biopsy determine prognosis and likelihood of response to treatment. In addition, kidney biopsy can be performed to help assess genetic diseases.

Prognosis based on renal pathology alone may be influenced by sample size and may not be absolute in biopsies with less glomeruli (i.e., ≤5). Renal biopsy should always be interpreted along with clinical and laboratory features. Chronic changes (interstitial fibrosis and tubular atrophy) indicate magnitude and duration of prior injury.

The following article provides an overview of issues concerned with percutaneous renal biopsy.

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2. Overview

Renal biopsy involves examination of the tissue under light, immunofluorescence (and immunoperoxidase in some laboratories),[3] and electron microscopy. The routine immunofluorescence examination of biopsy specimens should include evaluation of IgG, IgM, IgA, C3, C1q, albumin, fibrin, and kappa and lambda immunoglobulin light chains. Special studies, including evaluation of serum amyloid A deposits, IgG subclasses (IgG1-4), and collagen chains (alpha 3.4 and 5). A study of 288 native renal biopsies performed over a 6-month period in 1996 examined the diagnostic findings provided by light, immunofluorescence, and electron microscopy.[4] In this study, electron microscopy provided required diagnostic information in 21% cases and important confirmatory data in 21% cases.

2.1. Indications and when biopsy may not be essential

The indications for performing a renal biopsy vary among nephrologists. The utility of the biopsy may differ considerably based upon the indication. Older age per se is not a contraindication to renal biopsy. The following discussion will review the indications for renal biopsy according to the clinical presentation.

2.2. Isolated glomerular hematuria

In patients with asymptomatic microscopic hematuria (microscopic hematuria with dysmorphic red blood cells, negative "dipstick" for proteinuria, normal blood pressure and normal serum creatinine concentration), the renal biopsy usually does not alter therapy, because such patients generally have a good prognosis. When in such cases biopsy is performed, it usually demonstrates either a normal kidney biopsy or one of three disorders: IgA nephropathy, hereditary nephritis (Alport syndrome), or thin basement membrane disease. Most patients with IgA nephropathy and thin basement membrane disease without proteinuria have a good long-term prognosis and, other than angiotensin-converting enzyme inhibitors, there is no other available effective therapy for any of these conditions. However, some patients (such as those with Alport syndrome) may need histologic diagnosis for genetic counseling purposes. In a prospective study of 276 native renal biopsies, biopsy for isolated hematuria changed a management decision in only 1 of 36 patients.[5] Thus a renal biopsy is not usually done to establish a specific diagnosis, unless there is coexisting proteinuria or evidence of renal insufficiency.[6]

2.3. Isolated non-nephrotic proteinuria

A renal biopsy generally is not performed in a patient, who have with mild proteinuria (less than 500–1000 mg/day), absence of glomerular hematuria, normal renal function, and an absence of serologic or clinical evidence of a systemic disease that can cause glomerulonephritis (e.g., systemic lupus erythematosus). Some of such patients will have, IgA nephropathy, mild primary focal segmental glomerulosclerosis or membranous nephropathy.[7] Other patients may have secondary focal segmental glomerulosclerosis as a response to nephron loss (as in reflux nephropathy) or to ischemic injury (as in nephrosclerosis). Some nephrologists routinely perform a routine renal biopsy in patients with higher degrees of non-nephrotic proteinuria (1–2 g/day), except in the explained setting such as longstanding diabetes mellitus or hypertension.

2.4. Nephrotic syndrome

Renal biopsy is usually performed in most adults and older children with apparently idiopathic nephrotic syndrome. In this setting, one of the three major causes of idiopathic nephrotic syndrome is present: minimal change disease, focal segmental glomerulosclerosis, or membranous nephropathy. In one study, renal biopsy for nephrotic syndrome in adults influenced the management decision in 86% of cases.[5] Biopsy is usually performed in patients with active lupus nephritis to determine the type of disease that is present.

In contrast, there are a variety of patients with the nephrotic syndrome, in whom renal biopsy is usually not performed at diagnosis. It includes

1) Patients with long standing diabetes mellitus, in whom the initial manifestation is moderately increased albuminuria that slowly progresses to overt proteinuria over many years.
2) Patients with nephrotic syndrome that seems, from extrarenal involvement, to be due to primary or secondary amyloidosis, which can be diagnosed by lesser invasive tissue biopsy (such as abdominal fat pad or rectal biopsy).
3) Children under 6 years of age with acute onset of nephrotic syndrome, since more than 90% have minimal change disease.
4) Patients with relapse of steroid-sensitive nephrotic syndrome following the stoppage of appropriate immunosuppressive therapy, such as frequently relapsing minimal change disease.
5) Patients with overt (already diagnosed) malignancy. Usually common and major associations are membranous nephropathy with solid tumors and less often a hematologic malignancy such was chronic lymphocytic leukemia; and minimal change disease with lymphoma or leukemia. In these settings, the nephrotic syndrome often resolves with effective treatment of the malignancy.
6) Patients with massive obesity, who have slowly increasing proteinuria over time that is often subnephrotic rather than the abrupt onset of nephrotic syndrome. These patients usually have underlying secondary focal segmental glomerulosclerosis. The proteinuria in such patients with secondary FSGS often improves with weight loss.

2.5. Acute nephritic syndrome

The acute nephritic syndrome is usually caused by a systemic disease that needs a renal biopsy to establish the diagnosis and guide treatment. However, there are some situations, in which treatment is required while awaiting for the renal biopsy. It includes microscopic polyangiitis, granulomatosis with polyangiitis (Wegener's), or anti-GBM antibody disease. These disorders are usually associated with rapidly progressive glomerulonephritis and are suggested serologically by the presence of circulating antineutrophil cytoplasmic antibodies (ANCA) or anti-GBM antibodies. The reason for renal biopsy is variable in lupus nephritis. Patients with acute renal impairment and an active urinary sediment may have number of lesions and require a renal biopsy to establish a diagnosis, know prognosis, and guide therapy. A repeat biopsy may also be performed for late progression of the disease to distinguish between active lupus and scarring of previous inflammatory injury. Glomerulonephritis also may be associated with hepatitis C or B virus or with positive cultures for fungi or parasites or a chronic bacterial abscess.

Renal biopsy is usually not done in patients with a presumptive diagnosis of poststreptococcal glomerulonephritis based upon typical history of skin infection, recent pharyngitis and a positive throat or skin culture for group A beta-hemolytic streptococcal infection. Renal biopsy should be performed if there are recurrent episodes of hematuria, which is suggestive of IgA nephropathy or persistent hypocomplementemia at 6 weeks after appropriate therapy, and/or a progressive increase in serum creatinine.