The Kidney Biopsy in Lupus Nephritis: Is It Still Relevant?

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KEYWORDS

• Lupus nephritis • Kidney biopsy • Systemic lupus erythematosus

KEY POINTS

- The kidney biopsy is the standard of care for diagnosis of lupus nephritis and remains necessary to ensure accurate diagnosis and guide treatment.
- Repeat biopsy should be considered when therapy modifications are necessary, as in cases with incomplete or no response, or when stopping therapy for those in remission.
- There are several promising biomarkers of kidney disorders; however, these markers needed to be validated in a prospective clinical trial before being applied clinically.
- Molecular analysis may provide the information presently lacking from current evaluation of kidney disorders and may better inform prognosis and treatment considerations.

INTRODUCTION

The percutaneous kidney biopsy was introduced in the 1940s and incorporated into clinical practice in the 1950s.[1,2] This procedure, along with advances in the histopathologic examination of kidney tissue such as immunofluorescence and electron microscopy, greatly enhanced understanding of the pathogenesis of human glomerulonephritis. Perhaps more than for any of the other glomerular diseases, biopsy findings have been used to classify and subgroup lupus nephritis (LN) in order to inform treatment decisions and predict prognosis. Several LN classification schemes have been applied clinically, the most recent being from collaboration between the International Society of Nephrology and the Renal Pathology Society in 2004.[3] In an effort to forecast kidney outcomes, pathologic findings in LN have also been combined into composite indices of active and chronic disease independent of LN class.[4,5]

The role of the kidney biopsy in LN has recently been challenged on several fronts: (1) the widespread clinical practice of using mycophenolate mofetil (MMF) for

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induction treatment of proliferative and membranous LN has led many clinicians to question the need for diagnostic biopsies to guide therapy. (2) Diagnostic biopsies do not predict treatment response or long-term kidney outcomes in LN, and the added value of serial biopsies remains unclear. (3) Noninvasive biomarkers of renal disorders are actively being sought to substitute for invasive kidney biopsies. (4) The kidney biopsy is still only analyzed histologically, whereas molecular diagnostics are being applied to biopsies of other diseases to personalize therapy.

In light of these challenges, this article reexamines the kidney biopsy in LN in order to assess its ongoing relevance to disease management, and considers how molecular analyses can increase the information derived from the kidney biopsy.

WHEN AND HOW OFTEN DOES A PATIENT WITH LN NEED A KIDNEY BIOPSY?

An evidence-based literature has developed around this question, but to date there is no consensus answer. Three possible responses are considered here.

1. A kidney biopsy should routinely be obtained to confirm the diagnosis of LN before treatment is started.

This traditional approach is used when patients with systemic lupus erythematosus (SLE) develop clinical evidence that is consistent with renal involvement by lupus and that cannot be explained by other conditions. These clinical findings include hematuria, pyuria, red and white blood cell casts, declining kidney function, and/or proteinuria.[6] Dysmorphic red blood cells, specifically acanthocytes (**Fig. 1**), indicate glomerular hematuria and are often seen in the urine sediment of patients with LN with active nephritis. Red blood cell casts (see **Fig. 1**) also indicate glomerular hematuria, but are found less commonly. Urine white blood cells and white blood cell casts, in the absence of kidney or urinary tract infection, are consistent with kidney inflammation caused by LN. A kidney biopsy is generally not indicated for hematuria or pyuria alone, but patients who develop active urine sediment require close follow-up for signs of worsening kidney injury such as proteinuria and an increase in serum creatinine.

Besides LN, the differential diagnosis of renal dysfunction in patients with SLE includes tubular injury caused by systemic infection or nephrotoxins. Patients with lupus are susceptible to infection because they are routinely immunosuppressed, and often

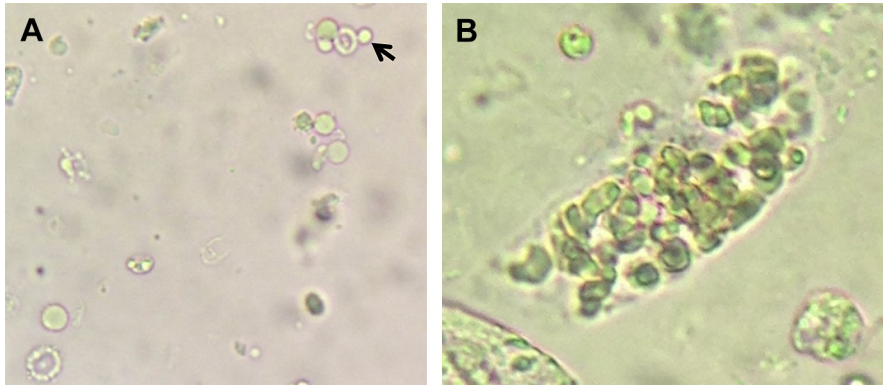

Fig. 1. Urine findings of glomerular hematuria in LN. (*A*) Acanthocytes are a type of dysmorphic red blood cell that is specific for glomerular hematuria. The arrow indicates a bleb that distorts the normal biconcave disc appearance of the red blood cell. (*B*) Red blood cell casts also indicate glomerular bleeding.