Renal involvement in systemic lupus erythematosus: glomerular pathology, classification, and future directions

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Abstract

Systemic lupus erythematosus is a common cause of glomerulonephritis. Despite improvements in the management of lupus nephritis, about 10–30% of patients develop end-stage kidney disease within 15 years. The renal biopsy provides crucial information to the clinician, as the choice of treatment is guided by the histopathologic findings. The light microscopic appearances and clinical features of patients with systemic lupus erythematosus can vary considerably, reflecting the many patterns of histopathologic injury seen in this glomerulonephritis. This review illustrates the glomerular pathology and pathogenesis of lupus glomerulonephritis, and will focus on the most recent classification, the International Society of Nephrology/Renal Pathology Society (ISN/RPS) 2003 Classification of Lupus Nephritis.

Keywords ISN/RPS classification; lupus nephritis; lupus pathology

Introduction

Systemic lupus erythematosus (SLE) is a systemic autoimmune disorder characterized by a female predominance and frequent development of glomerulonephritis.[1] Renal involvement in SLE remains the strongest predictor of overall patient morbidity and mortality. Renal involvement occurs in 20–49% of patients during their disease course.[1] The renal biopsy is critical in the management of SLE and answers important questions concerning the current status and the long-term prognosis of the kidney and the patient with SLE by providing a direct assessment of renal involvement that is independent of the clinical findings and that cannot be accurately predicted on the basis of clinical manifestations.[2] Because SLE can involve any renal compartment (glomeruli, tubulointerstitium, blood vessels), the biopsy establishes the site of injury. In addition, the most recent classification of lupus nephritis developed by the International Society of Nephrology and the Renal Pathology Society (ISN/RPS)[3] allows assignment of lesion specific therapy and prognostication.

This review will attempt to illustrate the renal pathology of lupus glomerulonephritis, summarize the 2003 ISN/RPS classification of lupus nephritis, and describe the pathogenesis of lupus glomerulonephritis.

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Glomerular pathology

The major histologic abnormalities of the glomerulus in lupus nephritis include immune deposits, glomerular proliferation, influx of leukocytes, glomerular necrosis, and scarring.[2] These basic types of renal lesions will be reviewed followed by a more detailed consideration of the ISN/RPS classification.

Wire loop

Wire loops, a classic sign of active lupus nephritis, are segmental areas of refractile, eosinophilic, thickening of the glomerular capillary seen by light microscopy in hematoxylin and eosin stained sections[4] (Figure 1). They correspond to massive subendothelial electron-dense deposits on electron microscopy (Figure 2), that when large enough to completely involve the peripheral circumference of the glomerular capillary wall, they may be detected by light microscopy forming wire-loop thickening of the glomerular capillary.

Hyaline thrombi

Hyaline thrombi are large, acellular, eosinophilic, intracapillary deposits which occlude the glomerular capillary lumens (Figure 3). The term is actually a misnomer because they do not represent true fibrin thrombi but are instead massive intracapillary immune deposits[2] (Figure 4).

Hypercellularity

Proliferation of glomerular endothelial, mesangial, and epithelial cells and infiltration of leukocytes is the most frequent histological finding in lupus nephritis.[5] Mesangial hypercellularity is usually accompanied by mesangial matrix expansion. Mesangial hypercellularity and matrix expansion are the first observable responses to mesangial deposits. Although it varies in intensity, isolated mesangial hypercellularity is associated with mild forms of lupus nephritis. The endocapillary hypercellularity results from the proliferation of glomerular endothelial and mesangial cells, as well as by leukocyte infiltration that occludes the glomerular capillary (Figure 5).

Crescents

Cellular crescents (Figure 6) are a feature of active lupus nephritis.[2,3] Cellular crescents commonly overlie necrosis of the glomerular tuft, and are formed by proliferating parietal epithelial cells with infiltrating mononuclear cells (monocytes or macrophages). The greater the proportion of glomerular involvement, the worse the prognosis, and when more than 50% are involved (crescentic glomerulonephritis), the renal prognosis is very poor.[5] With evolution of the glomerular injury, there is progressive scarring of cellular crescents, forming fibrocellular and fibrous crescents.

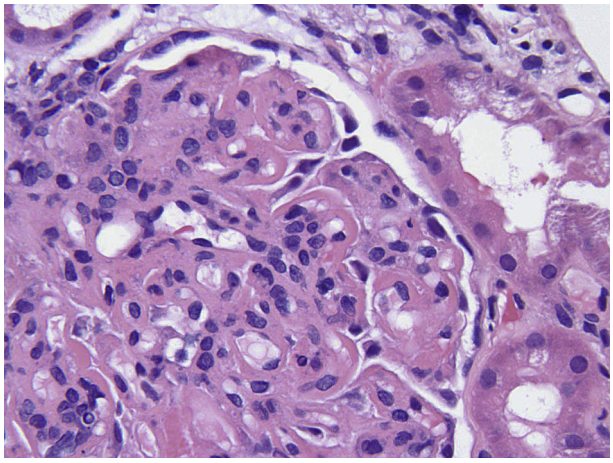

Figure 1 Wire loop. Glomerular capillary walls are thickened by wire-loop deposits showing rigid, band-like thickening of the glomerular basement membranes by intensely eosinophilic, glassy material corresponding to subendothelial deposits. (Hematoxylin and eosin stain).

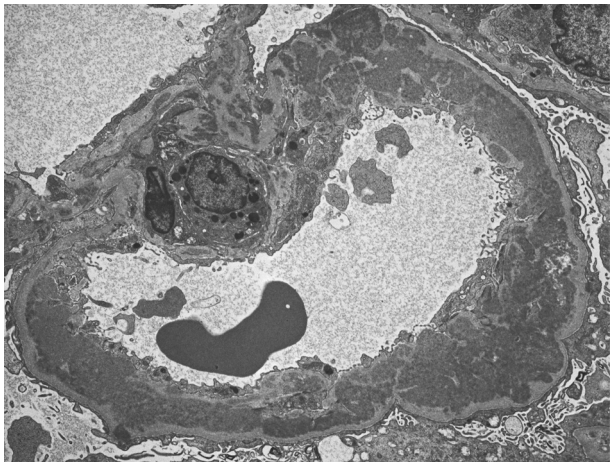

Figure 2 Wire loop. As illustrated in this electron micrograph, the wire loop represents large subendothelial electron-dense deposits composed of immune complexes.

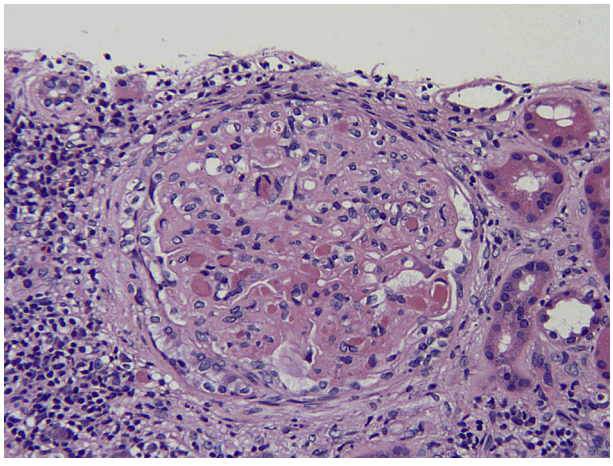

Figure 3 Hyaline thrombi. Several glomerular capillaries contain hyaline thrombi consisting of intraluminal immune deposits that form rounded, eosinophilic, intracapillary masses. (Hematoxylin and eosin stain).

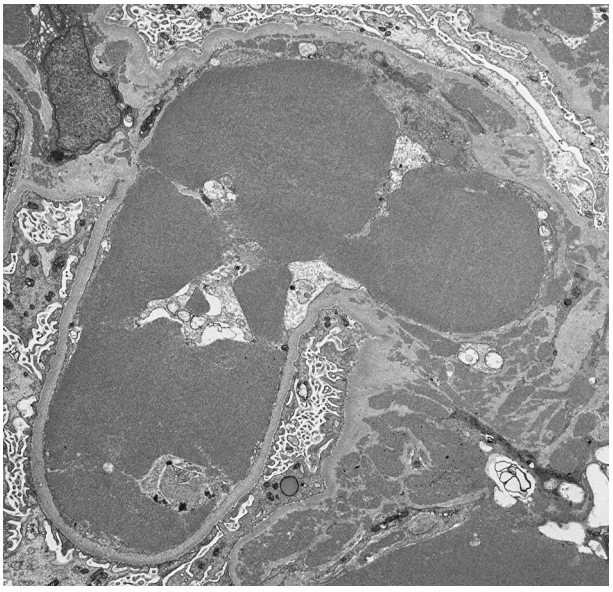

Figure 4 Hyaline thrombus. As illustrated in this electron micrograph, a hyaline thrombus consists of massive intracapillary immune deposits which occlude the glomerular capillary lumen.

Necrosis

Glomerular necrosis (Figure 7) is a destructive inflammatory lesion that heals with scarring and is frequently associated with crescent formation. The histological diagnosis of necrosis is established by the presence of fibrin, ruptures (breaks) of the glomerular basement membrane, and neutrophilic infiltrates with karyorrhexis. Karyorrhexis refers to apoptosis of infiltrating neutrophils producing pyknotic and fragmented nuclear debris ("nuclear dust").[2]

Glomerular sclerosis

Global or segmental glomerular scars result from severe or prolonged glomerular damage in the course of "active" glomerular lesions.[5] Because lupus nephritis is typically a remitting and relapsing condition with repeated episodes of reactivation, it is not

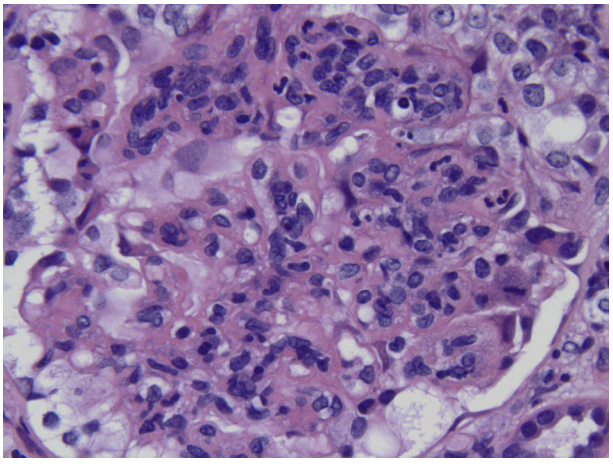

Figure 5 Endocapillary proliferation. Glomerular capillary lumens are occluded by global endocapillary proliferation. The cells include endothelial and mesangial cells and infiltrating leukocytes. (Hematoxylin and eosin stain).