Case #19

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NIEHS
Morphologic Diagnoses

1. **Kidney:**
   - Marked, diffuse, segmental to global membranous glomerulonephritis and glomerulosclerosis with thrombosis;
   - Marked, diffuse, lymphoplasmaacytic interstitial nephritis with tubular degeneration, proteinosis, and cast formation;
   - Mild, multifocal, fibrinoid vascular necrosis.

2. **Lymph nodes:** Moderate, diffuse lymphoid hyperplasia and plasmacytosis; Marked, multifocal, fibrinoid vascular necrosis.

3. **Spleen:** Moderate, diffuse, lymphoid hyperplasia and plasmacytosis; Marked, multifocal fibrinoid vascular necrosis.

4. **Aorta:** Marked, diffuse, fibrinoid vascular necrosis with granulation and hemorrhage.

5. **Heart:** Moderate, focal, fibrinoid vascular necrosis and myocardial necrosis.
MRL/lpr transgenic mouse

• Model of human SLE

• Immune complex GN, vasculitis, sialoadenitis, arthritis by 12 wks of age

• Retroviral transposon insertion mutation in lpr gene (Fas)

• Lymphoproliferation, autoreactive T-cells, auto-antibodies, circulating immune complexes
Mechanism of lesions

Immune complex glomerulonephritis, vasculitis

Activation of glomerular mesangial cells

IL-1, TNF-α, IFN-γ, IL-12

Recruitment of inflammatory cells

IL-1, TNF-α, IFN-γ, IL-12

Damage to GBM, matrix production

Glomerulosclerosis

Chronic interstitial nephritis

Tubular damage and loss

Chronic renal failure

Tubular proteinosis and protein loss

Loss of antithrombin III

Systemic thrombosis and vascular necrosis
Questions?

References: