

Serologic testing in kidney diseases

Renal Diseases Related to Infectious Diseases:

HIV: primary HIV infection can be associated with glomerulonephritis. These patients would be antibody negative but the 24 antigen positive and positive HIV RNA. Most common lesion is HIV associated nephropathy: these patients are HIV antibody positive and have positive HIV RNA titers. They do not necessarily have low CD4 counts and do not necessarily have opportunistic infections

Hepatitis B: chronic hepatitis B surface antigen positive patients can develop glomerular diseases, either membranous glomerulopathy or membranoproliferative glomerulonephritis. Patients who are surface antibody positive do not have glomerular disease related to hepatitis B

Hepatitis C: increasingly recognized as a cause of membranoproliferative glomerulonephritis. Hepatitis C antibody will be positive and HCV RNA will be positive. These patients can develop cryoglobulinemia and many of the cryoglobulins are rheumatoid factors, such that rheumatoid factor may be positive. Many patients with glomerulonephritis related hepatitis C do not have cryoglobulinemia.

Bacterial Endocarditis: > 90% are blood culture positive. The continuous bacteremia, especially if subacute, can lead to immune complex production with glomerular deposition leading to nephritic or mixed nephritic/nephrotic urinary findings.

Secondary Syphilis: can be associated with membranous glomerulopathy. RPR positive.

Poststreptococcal Glomerulonephritis (post infectious glomerulonephritis): blood cultures are not positive. Throat culture or skin culture may be positive. Evidence of previous streptococcal infection: ASO titer positive (throat), anti-DNAase B positive (skin). Bacterial antigens activate alternative complement pathway: CH50 reduced, C3 reduced, C4 normal. Complement levels tend to return to normal within 8-12 weeks of onset. Occasionally, other bacterial infections can get similar presentation: visceral abscess

ANCA associated diseases: (usually presented as rapidly progressive glomerulonephritis)

C-ANCA: associated with Wegener's granulomatosis. When test is positive, confirmed by demonstrating positive anti-proteinase 3 antibody (anti-PR3). Remission associated with loss of C-ANCA. Active disease associated with elevated ESR and disease activity can be estimated by changes in ESR.

P-ANCA: associated with microscopic polyangiitis. Also seen with crescentic glomerulonephritis (without evidence of systemic vasculitis). When test is positive, confirmed by demonstrating anti-myeloperoxidase antibody (anti-MPO). The remission is associated with loss of P-ANCA

Anti-glomerular basement membrane antibodies (usually presented as RPGN)

complement levels are normal. Diseased remission associated with loss of anti-GBM antibody.

Serologic testing for systemic lupus erythematosus

evidence of inflammation: elevated ESR and CRP. Renal involvement will be evidenced by abnormal serum creatinine or abnormal urinalysis (proteinuria and/or hematuria)

- 95% with positive antinuclear antibody, most commonly speckled pattern but maybe homogenous
- positive ANA antibody alone is not diagnostic of lupus, many elderly patients have positive ANA in low titer, less than 1:64
- severe renal disease usually associated with anti-double-stranded DNA antibody
- anti-Smith antibody: very specific for lupus insensitive
- homogenous pattern antinuclear antibody, usually anti-histone
- antibodies and may be drug-related (hydralazine, procainamide, isoniazid). Drug-related disease rarely involves the kidney

Sjogren's syndrome:

usually antinuclear antibody positive, typically speckled pattern
usually SS-A or SS-B positive

Mixed connective tissue disease

usually antinuclear antibody positive
very high titer anti-ribonuclear antibody (anti-RNP)
severe renal involvement is much less common, compared to lupus

Use of complement testing:

typical assessment includes CH50 (total hemolytic complement activity), C3, C4
classical complement pathway activates C4 as well as C3. This can lead to low C3 and C4 levels which lead to decreased CH 50. This would typically be seen with complement activation driven by immune complexes (lupus, hepatitis C, cryoglobulinemia)
alternative complement pathway activation is typically driven by bacterial or microbial antigens: C3 is directly activity producing low C3 and decreased CH 50 C4 is normal.
C3 may also be directly activated by C3 nephritic factor which is an antibody which activates C3 convertase directly (associated with membranoproliferative marrow nephritis, type II- also described as dense deposit disease.
diseases which do not have bacterial/microbial antigens or circulating immune complex will typically have normal levels of serum complement and normal CH 50.
IgA nephritis does not cause low serum complements as IgA is a poor complement activator. ANCA diseases do not produce circulating immune complexes, for us, complement levels are normal. For unclear reasons, anti-GBM disease typically presents with normal complement levels

Multiple myeloma (plasma cell dyscrasia):

often associated with anemia, elevated ESR, hypercalcemia

screening tests include serum protein electrophoresis to define a monoclonal protein.

This test is rather nonspecific

more specific evidence of monoclonal protein can be obtained from immunoelectrophoresis (IEP) or immunofixation and electrophoresis (IFE) which can be done on both serum and urine to detect monoclonal proteins. IgG paraproteinemia is the most common monoclonal light chain.

Amyloidosis related to multiple myeloma, usually Lambda light chain

light chain deposition disease: usually related to Kappa light chain.

Neoplastic plasma cell dyscrasia in multiple myeloma can suppress normal plasma cells, leading to hypogammaglobulinemia (low levels of total IgM, Ig A, and low IgG)

Monoclonal gammopathy of unknown significance (MGUS) typically does not lead to the bone pain, hypercalcemia, anemia, amyloidosis, abnormal kidney function, or free light chain in the urine. In MGUS a monoclonal protein is usually present in smaller quantities (usually less than 1.0 gm/dl)