

Glomerulonephritis: Review Questions

Sri G. Yarlagadda, MD

Ursula C. Brewster, MD

QUESTIONS

Choose the single best answer for each question.

- A 35-year-old man with no past medical history presents to the emergency department (ED) with cough and shortness of breath that have been present for 1 week. He reports occasional blood-tinged sputum. He denies malaise, weight loss, fevers, or joint pain. Blood pressure is 140/80 mm Hg, heart rate is 80 bpm, and oxygen saturation is 97% on room air. Laboratory testing reveals a blood urea nitrogen (BUN) level of 48 mg/dL (normal, 11–23 mg/dL) and serum creatinine level of 3.5 mg/dL (normal, 0.6–1.2 mg/dL). Serum electrolytes are normal. Urinalysis reveals 1+ protein, moderate blood, 3 to 4 red blood cell casts, and 2 to 3 granular casts per high-power field. Chest radiograph shows infiltrates in both lungs. A spot urine protein/creatinine ratio is 0.6 g/mg. Enzyme-linked immunoassay for anti-glomerular basement membrane (GBM) antibodies is positive. A titer for antineutrophil cytoplasmic antibodies (ANCA) is undetectable. The patient undergoes a renal biopsy. Light microscopy reveals crescents in the glomeruli, and immunofluorescence reveals linear staining of IgG along the glomerular capillaries. What is the best management strategy for this patient?

 - Dialysis
 - Intravenous (IV) prednisolone
 - Observation
 - Plasma exchange, prednisone, and cyclophosphamide
- A 9-year-old boy presents to the ED with his mother with puffy eyes and scant urine. His general health has been good until 2 weeks ago when he developed a sore throat and swollen glands. An antibiotic was started at that time. He appears well except for facial swelling and edema in his feet. Blood pressure is 150/90 mm Hg. The remainder of the physical examination is normal. Laboratory testing reveals a serum creatinine level of 1.8 mg/dL, BUN of 35 mg/dL, albumin level of 3.2 g/dL (normal, 3.3–5.2 g/dL), serum complement C3 level of 80 mg/dL (normal, 100–233 mg/dL), serum complement C4 level of 25 mg/dL (normal, 14–18 mg/dL), anti-streptolysin O titer of 230 U (normal, < 200 U), and an antinuclear antibody titer of 1:20 (> 1:40 is abnormal). Urinalysis reveals 1+ protein, 10 to 20 red blood cells, 2 to 6 white blood cells, and occasional red blood cell casts. Urine protein is 2 g/24 hr. What is the next step in the management of this patient?

 - Diuretics and antihypertensive medication
 - IV prednisone
 - Kidney biopsy
 - Oral cyclophosphamide
- A 60-year-old man presents to the ED with a 6-week history of fatigue, myalgias, weight loss, and shortness of breath. Past medical history is significant for hypertension for 10 years. Urine output and blood pressure are normal. There is no skin rash, hepatomegaly, splenomegaly, or peripheral edema. Laboratory testing reveals a hemoglobin level of 10 g/dL (normal, 13–18 g/dL), BUN of 68 mg/dL, and serum creatinine level of 4.5 mg/dL. Serum electrolytes are normal. Serum creatinine 1 year ago was 0.9 mg/dL. Urinalysis shows 2+ protein, 15 to 20 red blood cells, 5 to 10 white blood cells, and a few erythrocyte casts and granular casts per high-power field. Complement levels are normal. Ultrasound of the kidneys reveals 11-cm kidneys bilaterally with no hydronephrosis. Chest radiograph reveals patchy infiltrates in both lungs suggestive of bilateral multilobar pneumonia. The patient received 2 L of normal saline with no improvement in serum creatinine. Results of testing for serum anti-GBM antibodies, ANCA, and antinuclear antibody, serum protein electrophoresis, and urine electrophoresis are pending. What is the next step in the management of this patient?

 - Emergent renal biopsy
 - Lung biopsy

Dr. Yarlagadda is a fellow, and Dr. Brewster is an assistant professor of medicine; both are at the Section of Nephrology, Yale University School of Medicine, New Haven, CT.

- (C) Nasal and sinus biopsies
- (D) Wait for results of serologic testing and continue supportive therapy

Questions 4 and 5 refer to the following case.

A 37-year-old man presents to the ED with painless swelling in both ankles and a 10-lb weight gain over the past 3 months. During a physical examination 1 year prior, 2+ protein was noted on dipstick urinalysis, but the patient denied further evaluation because he felt well. There is no family history of renal disease. Blood pressure is 120/80 mm Hg. Physical examination is notable for edema in his legs up to the mid thighs. Laboratory testing reveals a hemoglobin level of 14 g/dL, hematocrit of 42%, serum glucose level of 80 mg/dL, serum creatinine level of 1.1 mg/dL, BUN of 28 mg/dL, albumin level of 2.6 g/dL, serum total cholesterol level of 325 mg/dL (normal, < 200 mg/dL), and serum triglyceride level of 800 mg/dL (normal, < 160 mg/dL). Serum complement levels are within normal limits. Urinalysis demonstrates 4+ protein on dipstick. Urine microscopy reveals 0 to 2 erythrocytes, hyaline casts, oval fat bodies, and fatty casts. A spot protein/creatinine ratio is 6 g/mg. The patient undergoes a renal biopsy.

4. What is the most likely biopsy finding?

- (A) Acute postinfectious glomerulonephritis
- (B) Alport's syndrome
- (C) Crescentic glomerulonephritis
- (D) Membranous nephropathy

5. Renal biopsy results are as suspected. A careful inquiry into the use of nonsteroidal anti-inflammatory drugs and other drugs is negative. Serologic testing for hepatitis B and C is negative. An age-appropriate work-up for malignancy is negative. What is the next step in this patient's management?

- (A) Furosemide and an angiotensin-converting enzyme (ACE) inhibitor
- (B) Monthly albumin infusions
- (C) Oral prednisone
- (D) Warfarin

ANSWERS AND EXPLANATIONS

1. (D) Plasma exchange, prednisone, and cyclophosphamide. This patient has Goodpasture's syndrome, also known as anti-GBM antibody disease, a syndrome of glomerulonephritis, pulmonary hemorrhage, and circulating anti-GBM antibodies. Goodpasture's syndrome is 1 of the 3 major forms of rapidly progressive (crescentic) glomerulonephritis. Patients usually present with acute kidney injury, and urinalysis reveals

non-nephrotic range proteinuria with nephritic sediment. Pulmonary involvement is present in 70% of cases.¹ The presence of anti-GBM antibodies and linear IgG staining of the basement membrane, as seen in this patient, define the disorder. The treatment of choice for Goodpasture's syndrome is plasmapheresis with concurrent prednisone and cyclophosphamide. Plasmapheresis removes circulating anti-GBM antibodies and other mediators of inflammation, while immunosuppressive therapy reduces new antibody production. Duration of treatment is determined by attainment of clinical remission and disappearance of anti-GBM antibodies.¹ IV prednisolone alone would not sufficiently treat this patient, and he has no indication for dialysis. Observation without treatment will lead to rapid progression to end-stage renal disease and death.

2. (A) Diuretics and antihypertensive medication. This patient has acute poststreptococcal glomerulonephritis, an immune complex-mediated glomerulonephritis usually seen in children but also found in adults. Antibodies that form against streptococcal antigens localize on the glomerular capillary wall and activate the complement system, initiating an inflammatory response. Symptoms typically develop a few days to weeks after a pharyngeal or skin infection with nephritogenic strains of group A β -hemolytic streptococci. If clinical features typical for acute poststreptococcal glomerulonephritis (eg, hematuria, red blood cell casts, proteinuria [< 3 g] on urinalysis) are present with reduced total complement activity and C3 levels as well as evidence of prior streptococcal infection, biopsy is not required. Management of patients with acute poststreptococcal glomerulonephritis is generally supportive with diuretics and salt restriction to control edema and antihypertensive therapy to control blood pressure.² The disease presents once acute infection has already resolved; therefore, antibiotics to treat group A streptococcal infection are not usually necessary unless symptoms of active infection are still present. There is no evidence that immunosuppressive therapy with steroids is beneficial. The majority of children recover spontaneously, even those presenting with severe acute kidney injury. Prognosis is excellent with recovery of renal function in 6 weeks and serum complement levels returning to normal in 6 to 12 weeks. Persistently low complement levels should prompt evaluation for another cause of glomerulonephritis or systemic lupus erythematosus nephritis. Asymptomatic urinary abnormalities such as microscopic hematuria and

proteinuria may persist for up to 2 years from the acute presentation. Recurrence of acute poststreptococcal glomerulonephritis is rare.

3. **(A) Emergent renal biopsy.** This patient presented with rapid decline in renal function and nephritic sediment, which suggests rapidly progressive glomerulonephritis. Additionally, the pulmonary infiltrates found on this patient's chest radiograph raise suspicion for a pulmonary-renal syndrome. To confirm the suspected diagnosis, the patient should undergo emergent renal biopsy. Rapidly progressive glomerulonephritis is characterized by crescent formation on light microscopy of the renal biopsy specimen.³ Immunofluorescence microscopy can distinguish between the 3 types of rapidly progressive glomerulonephritis: (1) anti-GBM disease, (2) pauci-immune glomerulonephritis, and (3) immune complex disease. Immune complex disease is associated with low complement levels and is unlikely in this patient given his normal complement levels. Both anti-GBM disease and pauci-immune glomerulonephritis can present as pulmonary-renal syndromes. On serologic testing, anti-GBM antibodies are positive in anti-GBM disease, while ANCA is positive in pauci-immune glomerulonephritis. Although these 2 diseases can be distinguished based on serology, a renal biopsy is still required because many of the currently available assays are not sufficiently accurate and the potential toxicities of current therapies for both diseases are too great to rely on serologic results alone. In anti-GBM disease, immunofluorescence microscopy of the biopsy specimen will show linear deposition of IgG along the basement membrane, whereas immunofluorescence studies are negative in pauci-immune glomerulonephritis.

4. **(D) Membranous nephropathy.** Glomerular disease presents as 4 distinct clinical syndromes: nephritic syndrome, rapidly progressive glomerulonephritis, asymptomatic abnormalities on urinalysis, and nephrotic syndrome. The nephritic syndrome is characterized by the presence of hematuria, red blood cell casts on urinalysis, varying degrees of hypertension, and proteinuria (often < 3 g).⁴ Rapidly progressive glomerulonephritis is a variant of nephritic syndrome. Renal function deteriorates rapidly over

days to weeks and is characterized by cellular or fibrous crescents on biopsy. Asymptomatic abnormalities on urinalysis include hematuria or proteinuria on dipstick. Nephrotic syndrome is characterized by severe proteinuria (usually > 3 g), hypoalbuminemia, edema, and hyperlipidemia. Based on this patient's symptoms and results of urinalysis, he has membranous nephropathy, 1 of the primary renal diseases that presents as nephrotic syndrome. Other primary renal diseases that present as nephrotic syndrome include minimal change disease, focal segmental glomerulosclerosis, and occasionally membranoproliferative glomerulonephritis.

5. **(A) Furosemide and an ACE inhibitor.** Treatment of idiopathic membranous nephropathy remains controversial due to a high spontaneous remission rate. Without treatment, generally one third of patients spontaneously remit, one third progress to renal failure, and one third remain unchanged.⁵ However, several general principles apply to the management of these patients, including diuretics to control edema, angiotensin inhibition to reduce proteinuria, and correction of hyperlipidemia.⁵ In selected patients with risk factors for progressive disease, such as presence of glomerular scarring, elevated serum creatinine at presentation, and proteinuria greater than 8 g/day, immunosuppressive therapy should be considered; however, glucocorticosteroids alone are not beneficial. Glucocorticosteroids should be combined with alkylating agents or calcineurin inhibitors to attain remission. Warfarin is indicated in patients at high risk for thromboembolism with massive proteinuria and an albumin level less than 2 g/dL and is not the initial step in management of membranous nephropathy.

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