A 12-Year-Old Boy With Dyspnea, Hypertension, Hematuria, and Proteinuria

Case: A 12-year-old boy presented to the emergency department with progressive dyspnea for 1 week and bilateral periorbital edema for 1 day. On review of systems, he reported an upper respiratory tract infection 1 week before the onset of dyspnea. A review of vital signs showed a temperature of 99.8°F (37.7°C), heart rate of 99 beats/min, blood pressure of 167/117 mm Hg, respiratory rate of 22 breaths/min, and oxygen saturation of 99% on room air. In addition to periorbital edema, the patient appeared to have worsening dyspnea when he was placed supine.

The patient’s admission laboratory values revealed the following: sodium, 142 mmol/L; potassium, 4.4 mmol/L; chloride, 112 mmol/L; bicarbonate, 20 mmol/L; blood urea nitrogen, 11 mg/dL; creatinine, 0.63 mg/dL; and a normal complete blood cell count except for a hemoglobin level of 9.8 g/dL. Urinalysis with microscopy showed trace amounts of blood with 6 to 10 red blood cells (RBCs) per high-power field and 100 mg/dL of protein. Chest radiograph revealed pulmonary edema (Fig 1).

Question: What is the significance of hematuria and proteinuria in this patient with hypertension and pulmonary edema?

Discussion: Hematuria and proteinuria, along with hypertension, are highly suggestive of glomerulonephritis (GN).\(^1\) Assessment of RBC morphology may help determine whether hematuria is glomerular or nonglomerular in origin. Intact urinary RBCs suggest an anatomic urinary tract lesion or trauma, whereas dysmorphic RBCs and RBC casts suggest glomerular hematuria. A fresh urine specimen should be analyzed under the microscope promptly because RBC casts disintegrate within 1 hour of voiding.

In patients with suspected GN, the amount of proteinuria should be quantified to assess the severity of GN. Nephrotic-range proteinuria in children is defined as >40 mg/m² per hour, >3 g/1.73 m²/day, or >50 mg/kg per day of protein in the urine. Because a 24-hour urine collection can be cumbersome, a morning spot urine protein/creatinine ratio can be obtained instead and correlated with the amount of protein excreted in a 24-hour collection.\(^2\) Urine protein/creatinine ratio of >2 mg protein/mg creatinine is considered nephrotic-range proteinuria.

Case Continuation: Results of additional laboratory studies revealed an albumin level of 3.4 g/d, low levels of complement 3 (C3) (19 mg/dL [normal: 90–180 mg/dL]) and normal levels of complement 4 (C4) (21.6 mg/dL [normal: 10–40 mg/dL]). The urine protein/creatinine ratio was mildly elevated at 0.31 (normal: <0.2 in >2 years of age).

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KEY WORDS
glomerulonephritis, hypertensive emergency, hypertensive urgency, postinfectious glomerulonephritis, poststreptococcal glomerulonephritis

ABBREVIATIONS
ASO: antistreptolysin O
BP: blood pressure
GABHS: group A β-hemolytic streptococcus
GN: glomerulonephritis
PIGN: postinfectious glomerulonephritis
PSGN: poststreptococcal glomerulonephritis
RBC: red blood cell

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**Question:** What approach should be used in determining the cause of acute GN in children?

**Discussion:** The differential diagnosis of GN is broad. Therefore, it is prudent to take a systematic approach based on: (1) complement levels; (2) time course of onset; and (3) systemic manifestations or isolated kidney involvement. Figure 2 summarizes a diagnostic approach to acute GN.

Serum complements (C3 and C4) should be obtained once GN is recognized. Low levels of C3 and normal levels of C4 are associated with postinfectious glomerulonephritis (PIGN) and membranoproliferative glomerulonephritis (MPGN). Levels of both C3 and C4 are decreased in patients with subacute bacterial endocarditis, systemic lupus erythematosus, and cryoglobulinemia. Immunoglobulin A (IgA) nephropathy, antineutrophil cytoplasmic antibody–associated vasculitides, glomerular basement membrane antibody–associated GN, and IgA vasculitis (also known as Henoch-Schönlein purpura) are associated with normal complement levels.

The time course of onset may also help differentiate between the different types of GN. Although most causes of GN can have either an acute, subacute, or chronic presentation, some etiologies tend to present more acutely than others. Of the hypocomplementemic glomerulonephritides, PIGN and endocarditis usually have an acute to subacute presentation. MPGN and IgA nephropathy often present more subacute to chronic in nature.

The presence of isolated kidney involvement versus systemic manifestations can aid in determining the etiology of GN. Signs and symptoms of airway or pulmonary parenchymal disease, along with normal complement levels, should raise suspicion for antineutrophil cytoplasmic antibody–associated GN or glomerular basement membrane–associated GN. Systemic lupus erythematosus and endocarditis should be considered in patients with systemic and cutaneous manifestations. Finally, recurrent episodes of gross hematuria should raise suspicions for IgA nephropathy, MPGN, and Alport disease.

**Case Continuation:** Because our patient presented acutely with hypertension, pulmonary edema, hematuria, proteinuria, and decreased C3 levels, PIGN was the most likely diagnosis. The diagnosis was further supported by an elevated antistreptolysin O (ASO) titer of 427 IU/mL (normal: <150 IU/mL).

**Question:** What is the difference between poststreptococcal glomerulonephritis (PSGN) and PIGN?

**Discussion:** PSGN refers specifically to GN occurring after group A β-hemolytic streptococcus (GABHS) pharyngitis or skin infections; PIGN is a broader term referring to immune-mediated GN that generally occurs 1 to 3 weeks after the
inciting infection. Staphylococcus and Streptococcus pneumoniae infections have been implicated in the development of PIGN. The pathophysiologic process in PIGN is believed to be immune complex deposition in glomerular tufts; however, the exact antigen that triggers this response has yet to be determined.

The incidence of postinfectious GN has been decreasing in most industrialized countries; however, it remains high in developing countries and is associated with poor living conditions and low socioeconomic status. Although treatment of GABHS infections has not definitively been shown to prevent the development of PSGN, prophylactic treatment of household contacts is advisable to prevent transmission of nephritogenic strains of GABHS in communities in which there is a high prevalence of PSGN.

PSGN is the most common cause of acute GN in children worldwide. A total of 470,000 cases are reported annually, with a typical age range of 5 to 12 years. Recent streptococcal infection should be confirmed by use of elevated antibody titers against cell wall antigens and extracellular products of group A streptococci. Measurements of ASO, anti-deoxyribonuclease B, anti-hyaluronidase, anti-streptokinase, and/or anti-nicotinamide adenine dinucleotide are used to demonstrate previous streptococcal infection. ASO titers are up to 97% sensitive but only 80% specific for previous GABHS infection.

**Case Continuation:** Our patient was monitored in the PICU because his blood pressure (BP) was persistently elevated in the range of 150 to 180/100 to 120 mm Hg. He was treated with sublingual nifedipine and oral furosemide, and his BP improved to 140/90 mm Hg.

**Question:** How do you classify and manage hypertension in patients with acute GN?

**Discussion:** Secondary hypertension due to GN is classified in the same manner as primary pediatric hypertension. The severity of hypertension is classified as stage I (mild) or stage II (severe). Stage I hypertension is defined as systolic BP and/or diastolic BP in the 95th to 99th percentile for age, gender, and height. Stage II hypertension is defined as the systolic and/or diastolic BP ≥5 mm Hg above the 99th percentile. Hypertensive emergency is an acute change in BP above stage II with signs and symptoms of end-organ damage such as seizures, encephalopathy, kidney injury, papilledema, and heart failure.

In patients with PIGN, management of hypertension is supportive and targeted against complications such as fluid overload, which can be treated by using thiazide or loop diuretics. Oral nifedipine and intravenous nicardipine are commonly used in the hospital setting for hypertension because the safety and efficacy of these agents are well established in children. Angiotensin-converting enzyme inhibitors should be considered in patients with persistent hypertension and normal glomerular filtration rates because kidney hypoperfusion triggers activation of the renin-angiotensin-aldosterone system.

**Question:** What is the natural course and prognosis of patients with PIGN?

**Discussion:** The prognosis for patients with epidemic cases of PSGN is favorable. Although patients with PSGN caused by sporadic infections tend to have a poorer prognosis, the majority of cases recover fully with no long-term consequences. C3 values may take 2 to 3 months to normalize. Hypertension and edema resolve after 2 to 4 weeks, and proteinuria and hematuria resolve by 4 to 6 weeks, although microscopic hematuria can persist for up to 1 to 2 years. A renal biopsy should be considered in patients with progressive kidney injury, persistent hematuria, proteinuria, and/or hypertension beyond 4 to 6 weeks.

**Conclusions** GN should be suspected in children presenting with hypertension, fluid overload, hematuria, and proteinuria. The time course of onset and complement levels may help determine the etiology of GN. PIGN is the most common cause of acute GN in children. Management of hypertension in acute GN includes the use of oral medications such as diuretics for fluid overload and calcium channel blockers or angiotensin-converting enzyme inhibitors for hypertension despite adequate diuresis.

Our patient was discharged from the hospital after 3 days and continued on oral furosemide for 1 week and nifedipine for 1 month until his BP normalized. The periorbital edema resolved after 3 days. At the 1-month follow-up visit, proteinuria had resolved with 0 to 1 RBC per low-power field on urinalysis. Repeat C3 (90 mg/dL) and C4 (16.3 mg/dL) levels normalized 2 months after initial presentation.

**REFERENCES**


2. Lemann J Jr, Doumas BT. Proteinuria in health and disease assessed by measuring


