

Post-Infectious Glomerulonephritis Associated with Adenovirus Infection

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Post-infectious glomerulonephritis is the most common cause of acute glomerulonephritis in children [1]. The agents implicated include bacteria (mainly *Streptococcus*) [2], viruses (herpes simplex, hepatitis B, Epstein-Barr, cytomegalovirus) [1], fungi (*Histoplasma*) [2], and parasites [*Toxoplasma*, *Plasmodium* (malaria)] [1,2]. However, no association of PIGN with adenovirus infection has been described. We report a child with acute glomerulonephritis associated with adenovirus infection.

PATIENT DESCRIPTION

A 4 year old boy was admitted to our department with rhinitis, cough, fever and vomiting of 4 days duration, and macrohematuria, which appeared one day prior to his admission. His 3 year old sister had a febrile illness with respiratory symptoms 10 days earlier. His medical history was otherwise unremarkable.

On admission, temperature was 38.7°C, blood pressure 130/80 mmHg (which is 10 mmHg above the 99th percentile for age and height), heart rate 130 beats/minute, and respiratory rate 35 breaths/minute. The tonsils were enlarged and hyperemic, but without exudates. Rhinorrhea was also present.

PIGN = post-infectious glomerulonephritis

Heart and lung examination revealed no abnormalities. There was no lymphadenopathy, hepatosplenomegaly, rash or edema.

Laboratory findings at admission were: C-reactive protein 8.3 mg/dl (normal < 0.5 mg/dl), hemoglobin 10.6 g/dl, white blood cell count 10,250/mm³ (neutrophils 79%, lymphocytes 10%, monocytes 8%, eosinophils 3%), and platelet count 215,000/mm³. Blood chemistry (SMA-18) was normal except for creatinine 0.9 mg/dl (normal for this age, up to 0.7), and urea 64 mg/dl (normal 10–50). Urinalysis revealed numerous erythrocytes and erythrocyte casts without leukocyturia. Twenty-four hour urine collection showed normal range proteinuria of 200 mg/24 hr. Chest X-ray demonstrated right lower lobe infiltrates. Abdominal sonography showed enlarged kidneys with increased parenchymal echogenicity.

Rhinitis, tonsillitis, pneumonia and acute glomerulonephritis were diagnosed. Intravenous cefuroxime (100 mg/kg/day) was initiated. However, cough, fever, tonsillar hyperemia and lung infiltrates persisted for 10 days, denoting no improvement of the pneumonia or the tonsillitis. Repeated chest X-ray on day 11 of hospitalization showed right middle and right upper lobe infiltrates. Oral azithromycin (10 mg/kg) was added to the treatment to cover atypical organisms. Gradual improvement occurred over the next few days: blood pressure normalized (110/60 mmHg) and creatinine level decreased to 0.5 mg/dl; however, microhematuria persisted.

Additional investigations showed C3 of 43 mg/dl (normal 90–200 mg/

dl), C4 72 mg/dl (normal 16–48 mg/dl) and CH50 42% (normal 50–150%). Immunoglobulin-G was 1880 mg/dl (normal 550–1350 mg/dl), IgA 160 mg/dl (normal 50–210 mg/dl) and IgM 130 mg/dl (normal 60–200 mg/dl). Blood cultures were negative. Antistreptolysin titer, antinuclear antibodies, anti-ds-DNA, antiglomerular basement membrane antibodies, anticytoplasmic antibodies, serology for cytomegalovirus, Epstein-Barr virus, *Mycoplasma*, *Chlamydia pneumoniae* and *Chlamydia psittaci* were all normal or negative. Throat culture yielded adenovirus; however, the culture for serotyping was contaminated.

The patient was discharged after 2 weeks. At follow-up after 2 months he was asymptomatic and without hematuria. Repeated test for antistreptolysin titer was negative. C3 was normal (105 mg/dl), as were the urinalysis results.

COMMENT

Our patient presented with the typical clinical features of PIGN, namely, macrohematuria, red blood cell casts in the urine, hypertension, elevated blood levels of creatinine and urea, low levels of C3, and normal C4. There was no evidence of streptococcal infection. The only pathogen isolated was adenovirus from a throat culture. The typical accompanying clinical features of adenovirus infection, including rhinitis, pharyngitis and pneumonia, were also present. There were no symptoms to support the diagnosis of cystitis,

IgA = immunoglobulin A

such as dysuria or leukocyturia, and no evidence of autoimmune diseases. The rapid resolution of the disease, including the hematuria and hypertension, and normalization of blood C3 levels, supported the diagnosis of PIGN.

Human adenovirus is a large group of DNA viruses among which approximately 40 stereotypes cause diseases in humans, especially infections of the respiratory and gastrointestinal systems, and conjunctivitis. Other clinical syndromes related to adenovirus infections include meningoencephalitis, and fatal disseminated infection in immunocompromised hosts [3]. Adenoviruses, mainly serotypes 7, 11 and 21, are also associated with hemorrhagic cystitis, which manifests with gross hematuria and dysuria. In patients after chemotherapy or renal transplantation, adenovirus serotypes 34 or 35 infections were associated with necrotizing tubulo-interstitial nephritis [3]. We did not find any reports in the literature of an association of acute adenovirus infections and post-infectious glomerulonephritis.

The pathogenesis of PIGN is not fully understood. Most forms of glomerulonephritis are considered to be a consequence of an immunological process. The leading theory is that inflammation of the kidney is caused by binding or deposition of antigens in the glomeruli, further stimulating fixation of complement and specific antibodies with accumulation of various inflammatory cells.

The clinical course of post-streptococcal glomerulonephritis is well known, but data of glomerulonephritis follow-

ing other types of infection are scarce. Post-streptococcal glomerulonephritis is manifested by gross hematuria, red blood cell casts and dysmorphic irregular blood cells in the urine sediment, mild proteinuria, azotemia, oliguria, edema, and hypertension. Most patients have decreased levels of C3, properdin and/or C5 during the acute phase of the disease and normal or increased levels of C4, indicating activation of the alternative complement pathway. The latency period between the infection and the onset of nephritis in post-streptococcal glomerulonephritis is 1–4 weeks. In other types of PIGNs, the length of the latency period differs and is usually shorter [1]. In acute glomerulonephritis associated with non-streptococcal infections, the nephritis is usually milder and often is manifested only by hematuria and proteinuria rather than the fully developed syndrome with edema and hypertension. The outcome of post-streptococcal glomerulonephritis is usually good, rarely resulting in permanent renal dysfunction [1]. There is not enough information regarding the prognosis of PIGN following other pathogens. It was reported that in some cases, such as *Mycoplasma* infection, the process of destructive glomerular proliferation persists until the source of infection is eradicated [4].

Several patients with pneumonia-associated glomerulonephritis have been reported [5]. Most had bacterial infections, mainly streptococcal. Other reported pathogens included *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Chlamydia pneumoniae*,

Mycoplasma pneumoniae, *Coxiella burnetii* and *Nocardia*. A short latency period of several days (usually less than a week) has been observed. Transient hypocomplementemia was common. Histological study shows deposits of immune complexes in the glomerulus. Prognosis was good.

In view of the clinical course and the comprehensive workup, we concluded that our patient had post-adenovirus glomerulonephritis. To our best knowledge this is the first report of a child with PIGN associated with an adenoviral infection.

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“The sorrow which has no vent in tears may make other organs weep”

Henry Maudsley (1835-1918), British psychiatrist who established the Maudsley Hospital after his wife died because there was no suitable treatment for her condition. The hospital is still running today. He was one of the first editors of what's known today as *the British Journal of Psychiatry*. It was Maudsley who helped expand the scope of the journal to include articles of both a psychological and philosophical nature

“We must embrace pain and burn it as fuel for our journey”

Kenji Miyazawa (1896-1933), Japanese poet and children's story write