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CLINICAL VIGNETTE

Pauci-Immune Glomerulonephritis in an Elderly Patient with Dementia: Geriatric Considerations

Maija B. Sanna and Grace I. Chen

An 85-year-old female with known moderate dementia and osteoarthritis presented with her caregiver reporting decreased appetite and increased fatigue. At her baseline, she required 24-hour supervision for safety, but was ambulatory and cared for all of her own toileting needs. Donepezil was her only medication and had been increased two weeks earlier from 5mg daily to 10mg daily. Of note, her long-term partner had died one month prior to her presentation. There was no history of nausea or vomiting, change in bowel or urinary habits, cough, fevers, chills, or sweats. On physical exam, she had clear lungs and normal bowel sounds with a non-tender and non-distended abdomen. A comprehensive metabolic panel, complete blood count, and routine urinalysis were ordered, but the patient was unable to provide blood or urine samples that day. Donepezil was reduced from 10mg to 5mg daily given possibility of medication side effect contributing to her symptoms.

The patient's fatigue and decreased appetite persisted. She subsequently developed upper respiratory symptoms with dry cough, sneezing, and rhinorrhea. Two weeks after her initial presentation to the clinic, she completed her blood work. Her complete blood count was remarkable for new anemia with hemoglobin of 10.8 g/dL. The white blood cell count was normal but had borderline lymphopenia with an absolute lymphocyte count of 1.2 x 10E3/μL (reference 1.3-3.4 x 10E3/μL) and borderline elevated absolute monocyte count of 1.1 x 10E3/μL (reference 0.2-0.8 x 10E3/μL). There was no eosinophilia. Platelet count, liver enzyme levels, and electrolytes were within normal limits. Her creatinine was elevated at 2.7 mg/dL, with blood urea nitrogen of 33 mg/dL (baseline 6 months earlier was creatinine 0.7 mg/dL and urea nitrogen of 27 mg/dL). Urinalysis was significant for gross hematuria with 2+ protein, 3+ blood, 3+ leukocyte esterase, 829 red blood cells, 621 white blood cells, and 74 squamous cells. Repeat testing confirmed elevated creatinine and hematuria. Given her recent decreased appetite, she was given a liter of intravenous fluids to see if hypovolemia was contributing to her acute renal insufficiency. Repeat blood work after fluid challenge showed no improvement in her creatinine. A CT scan of the kidneys, ureter, and bladder showed no mass or renal abnormality; the patient was admitted for renal biopsy and further evaluation.

On admission, her cough had worsened, she had a fever, and her creatinine had increased to 3.2 mg/dL. Chest x-ray showed peri-bronchial thickening; she was initiated on antibiotics for possible community acquired pneumonia. Respiratory viral culture panel returned positive for human metapneumovirus, her respiratory symptoms improved and antibiotics were discontinued on hospital day three. She subsequently developed *Clostridium difficile* diarrhea and was started on metronidazole. Serologic testing was negative for antinuclear antibody, rheumatoid factor, C-ANCA, myeloperoxidase antibody, and proteinase 3 antibody, but the P-ANCA returned positive at 1:80. Her kidney biopsy showed pauci-immune crescentic glomerulonephritis with moderate tubulointerstitial changes confirming the diagnosis of rapid progressive glomerulonephritis (RPGN) of the pauci-immune type.

Treatment for RPGN was initiated with steroids (3 days of intravenous methylprednisolone followed by oral prednisone 60mg daily). She developed hemoptysis with hypoxemia, raising concern for diffuse alveolar hemorrhage (DAH). Diagnostic bronchoscopy was considered but was not consistent with the patient's goals. She was treated for health care associated pneumonia (HCAP), and her hospital course was further complicated by steroid-induced delirium. After completion of antibiotics for HCAP and a subsequent *Clostridium difficile* stool infection, she received rituximab for her RPGN.

Discussion

The incidence of acute kidney injury (AKI) increases with age.[1] The differential diagnosis for an elderly patient presenting with AKI is broad. Pre-renal etiologies, including dehydration and decompensated congestive heart failure, are common in geriatric patients.[2,3] Obstruction along the urinary tract, as is seen in prostatic disease, is also common in the geriatric population.[1] Intrinsic renal disease can be from acute glomerulonephritis, acute interstitial nephritis (AIN), acute tubular necrosis (ATN), and cholesterol emboli.[1]

Polypharmacy is common in geriatric patients[4] and medications can contribute to AKI via different mechanisms. NSAIDs and renin-angiotensin system blockers can lead to AKI through alterations in renal vascular auto-regulation. Medications known to cause AIN include diuretics, NSAIDs, proton pump inhibitors, allopurinol, and antibiotics.[1,5] Medications such as antibiotics and contrast agents can also contribute to AKI via ATN.[1]

RPGN is the most common form of acute glomerulonephritis in the elderly.[1] Presentation can range from acute macroscopic hematuria, oligouria, and edema to a more insidious onset with fatigue and edema. Laboratory findings include evidence of

decline in glomerular filtration rate and urinalysis shows dysmorphic hematuria, proteinuria, and casts.[6] Histology shows glomerular crescent formation.

There are three main types of RPGN classified by histology findings. Type I, or anti-glomerular basement membrane antibody glomerulonephritis, is characterized by presence of anti-glomerular basement membrane antibodies. Type II, or immune complex glomerulonephritis, is characterized by granular immune deposits, and can occur in IgA nephropathy, post-infectious glomerulonephritis, lupus nephritis, and mixed cryoglobulinemia. Type III RPGN, or pauci-immune glomerulonephritis, is a necrotizing glomerulonephritis characterized by a lack of immune deposits on histology and is the most common etiology of primary RPGN, representing 80% of cases.[7] Pauci-immune necrotizing glomerulonephritis can occur in conjunction with other organ involvement in both microscopic polyangiitis and granulomatosis with polyangiitis or can be renal-limited.[7] ANCA is positive in 75-80% of elderly patients with RPGN due to pauci-immune crescentic glomerulonephritis or microscopic polyangiitis.[6] Types II and III RPGN are more common than type I in the elderly.[1]

Without treatment, the prognosis of pauci-immune RPGN is poor and progression to end stage renal disease is typical within weeks to months. Older age at presentation, higher serum creatinine level, presence of pulmonary hemorrhage and dialysis dependence are associated with a less favorable prognosis.[7] While treatment with high dose intravenous methylprednisolone or cyclophosphamide typically improves renal function in the majority of patients, the elderly are at high risk for adverse effects of medications, associated infections, and intolerance.[6]

This case of AKI in an elderly patient highlights important geriatric considerations. First, the patient's underlying dementia likely contributed to delay in diagnosis. Although gross hematuria was present on her initial urinalysis, there was no clinical history of hematuria. She was able to independently use the bathroom and perhaps her dementia prevented her from recognizing the importance of hematuria and bringing it to the attention of her caregivers and/or doctor. Second, her symptoms of fatigue and decreased appetite are common in geriatric patients and could be explained by the recent loss of her life partner or increase in dose of donepezil. Third, it illustrates the importance of recognizing AKI caused by rapidly progressive glomerulonephritis. RPGN should be considered when an elderly patient presents with new onset kidney injury with hematuria and proteinuria. A prompt referral to a nephrologist should be pursued for a kidney biopsy and initiation of immunosuppressive medication(s). Risks and benefits of treatment need to be explored with the patient and/or surrogate decision maker given higher risk of medication side effects and infection with advanced age.

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