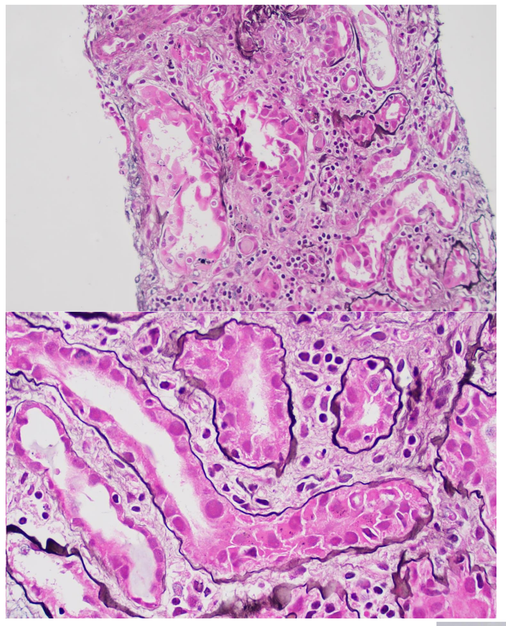
A peculiar presentation of concomitant pauci-immune glomerulonephritis with interstitial nephritis

KHADIJ ASSANI, DO[1]; RABIA SARWAR, MD[1]; DAVID HENRIQUEZ TICAS, MD[2]; MATTHEW J.NOVAK MD[3]; EUGENE DEGUZMAN MD[3]

1.DEPARTMENT OF INTERNAL MEDICINE, SKAGIT VALLEY HOSPITAL, WASHINGTON, USA
2. DEPARTMENT OF LABORATORY AND PATHOLOGY, UNIVERSITY OF WASHINGTON, WASHINGTON, USA
3. DEPARTMENT OF NEPHROLOGY, SKAGIT REGIONAL HEALTH, WASHINGTON, USA
3.

INTRODUCTION

Pauci-immune glomerulonephritis (PIGN) is often a rapidly progressing glomerulonephritis that commonly presents with acute kidney injury. This subset of glomerulonephritis is described as having little to no immune deposition within the glomerulus. PIGN is typically caused by systemic vasculitis as a majority of patients with renal limited vasculitis are often antineutrophil cytoplasmic antibody (ANCA) positive.[4] The most common vasculitides associated with PIGN are granulomatosis with polyangiitis, microscopic polyangiitis, and eosinophilic granulomatosis with polyangiitis[5]. Acute interstitial nephritis (AIN) is a well-known cause of acute kidney disease (AKD) and chronic kidney disease (CKD) and is associated with progression to end stage renal disease (ESRD). AIN is primarily an immune-mediated kidney injury triggered by use of certain medications, in particular antibiotics, PPIs, NSAIDs, and immune checkpoint inhibitors (ICPIs), or by autoimmune diseases, such as Sjogren syndrome, sarcoidosis, IgG4-related tubulointerstitial disease. In developed countries, medications are the most common cause of AIN (>70%), whereas the number approximates 50% in developing countries. On the other hand, there are a limited number of cases with MPO-ANCA associated vasculitis that presented as interstitial nephritis karyomegalic type, which is not linked to allergic reactions, but may be due to DNA damage (e.g., chemotherapeutics) or FAN1 mutations. We present an unusual case of pANCA vasculitis with concomitant karyomegalic interstitial nephritis.

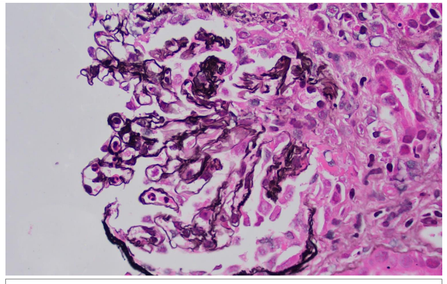


Slides 1 and 2: There is diffuse tubulitis with mononuclear cells infiltrating the epithelial cell layer. The tubules diffusely show acute injurious changes characterized by epithelial attenuation, sloughing of tubular epithelial cells into the lumen, and blebbing of apical epithelial cell cytoplasm. Tubules also show irregular nuclear features including hyperchromasia, nuclear enlargement, and occasional atypical nuclear chromatin pattern which appears alternately smudged or vesicular with central eosinophilic granules. Slide 1 and 2 : intermediate power and high power view of tubulointerstitial parenchyma, respectively

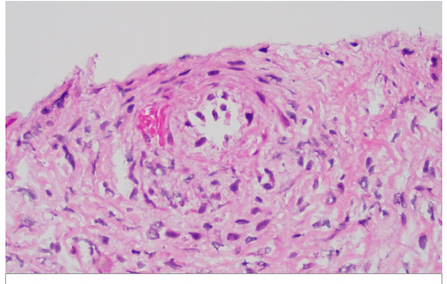
CASE

The case is of a 73-year-old female with a past medical history of Graves disease, hypertension, and hyperlipidemia presenting with loss of taste and smell, weakness, and myalgias for about 2 weeks. She subsequently had decreased appetite and poor oral intake. She believed she may have contracted COVID however denied any exposures or sick contacts. She does admit to shortness of breath with exertion and minimal watery diarrhea the day prior to admission. She denies any new medications, non-steroidal anti-inflammatory use, antibiotic use, or exposure to intravenous contrast. She denied orthopnea, urinary changes or symptoms, cough, chest pain, abdominal pain, flank pain, fever/chills, hematuria, or lower extremity swelling.

On presentation, she had severe acute kidney injury with urinalysis notable for moderate hematuria and leukocyte esterase with only trace proteinuria. Her COVID-19 test was negative. Urine sediment was most consistent with acute tubular necrosis and did not show any evidence of dysmorphic RBCs or RBC casts. Serologies were drawn and ANCA panel came back positive for perinuclear antibody and myeloperoxidase antibody. Her renal function worsened requiring initiation of hemodialysis. Renal biopsy showed findings consistent with PIGN but also diffuse interstitial nephritis which appeared out of proportion to her PIGN. Acutely injured tubules show bizarre nuclear atypia and enlargement which raised concern for viral infection but viral immunostains were negative. Viral testing including antibodies for COVID were negative during admission. She was given rituximab for induction therapy for her PIGN[2]. She was started on intravenous solumedrol 500mg daily for three days then transitioned to 80mg prednisone daily with a scheduled taper upon discharge. She remained hemodialysis dependent however showed improvement in her serum creatinine.



Slide 3: Focal necrosis of the glomerular hilum



Slide 4: Small artery in H&E stained screening section of frozen material with changes suspicious for fibrinoid necrosis of its wall

DISCUSSION

The objective of presenting this case is to bring under consideration the importance of kidney biopsy in determining the cause of unexplained acute kidney injury with picture consistent with acute tubular necrosis, glomerulonephritis and karyomegalic interstitial nephritis.

An unusual feature in this case which is observed is the presence of diffuse acute tubular injury and tubulointerstitial nephritis which appears out of proportion to the extent of glomerular involvement by necrotizing/crescentic lesions. Some of the acutely injured tubules show bizarre nuclear atypia and enlargement which raised concern for viral infection. However, immunostains for adenovirus, cytomegalovirus, and polyomavirus were all negative, making this possibility less likely. The histologic appearance of these injured tubules raised the possibility of karyomegalic interstitial nephritis, a rare form of tubulointerstitial injury that is associated with certain gene mutations (FAN1) and certain toxin/medication exposures (ifosfamide, ochratoxin)[67]. Further evaluation of clinical exposures/genetic susceptibility that may be driving this atypical tubulointerstitial inflammatory process may be helpful. Focus on key aspects of clinical and histologic diagnosis and management of patients suspected of having interstitial nephritis is an important first step. The field sorely needs useful clinical and laboratory criteria to confirm a clinical diagnosis. In the same vein, consensus histologic criteria are needed to determine a pathologic diagnosis of karyomegalic interstitial nephritis. Additionally, a consensus approach for prognosis and treatment of this type of interstitial nephritis that addresses issues of patient selection for immunosuppressive therapy, dose, and duration of therapy as well as predictors of prognosis is required.

In conclusion, this is a 73-year-old, previously healthy female, who presented in acute kidney injury and was found to have p-ANCA vasculitis with PIGN and interstitial nephritis with no apparent cause. Her case proved challenging as her clinical presentation was nonspecific and her urine sediment was inconsistent with glomerular pathology. This shows the importance of early renal biopsy and serologic testing in acute kidney injury without an otherwise obvious cause.

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