What is causing acute renal failure in my RA patient?

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Disclosure slide

Speakers bureau for AbbVie and Amgen

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History of LW

69 yo WF patient of mine since 2011 with history of overlap syndrome with RA, Sjogren's, scleroderma

- Predominantly inflammatory arthritis symptoms, fatigue and sicca
- Raynaud's and mild pulmonary hypertension, mild sclerodactyly
- Livedo reticularis with low titer positive IgM anticardiolipin antibodies,-LAC
- Photosensitivity, also eczema by biopsy
- Chronic renal insufficiency due to multiple UTI's as a child

Past medical history

- hypothyroidism
- migraine headaches
- interstitial cystitis
- asthma
- total knee replacement 3/2024

Labs at diagnosis

RF >100

Anti-CCP 86

ANA >1:2560, dsDNA neg, ENA neg

C3, C4 normal

Anticardiolipin outside positive but repeat negative

Creat 1.3 eGFR 51

UA trace blood, no protein or WBC

Prior DMARDS

-Azathioprine-elevated LFT's
-Mycophenolate mofetil-ineffective as a single agent
-MTX-contraindicated with renal disease
-Adalimumab-waning efficacy
-Etanercept-waning efficacy
-Abatacept-waning efficacy

-Sarilumab-started May 2024

Current medications

Mycophenolate mofetil 500 mg TID

Sarilumab 200 mg every other week

Triamcinolone cream as needed

Hydroxychloroquine 200 mg daily

Montelukast 10 mg daily

Omeprazole 40 mg daily

Nortriptyline 50 mg at bedtime

Losartan 50 mg daily

Albuterol inhaler, Advair inhaler

Cyclosporine eye drops

Vitamin D 1000 units daily

Levothyroxine 175 mcg daily

Clinical course 2024/2025

Feels great with switch to Sarilumab, gets monthly labs for MMF

10/17/2024 eGFR 41(about baseline), CBC normal including diff, urinalysis trace blood, 1-3 RBC's

11/14/2024 eGFR 24, CBC normal, urinalysis unchanged

11/21/2024 CMP showed BUN 43, creatinine 2.4 with EGFR 21, normal electrolytes
seen by her nephrologist, renal doppler fine

12/9/2024, eGFR 15, normal CBC and no change in urinalysis
ongoing workup with nephrology

1/6/2025 eGFR 9, WBC 14.5,Hgb 11.9, normal electrolytes and no change in UA
seen this day for acute R wrist arthritis, presumed gout with uric acid 9
treated with steroids, having some uremic symptoms of nausea

What would you do at this point?

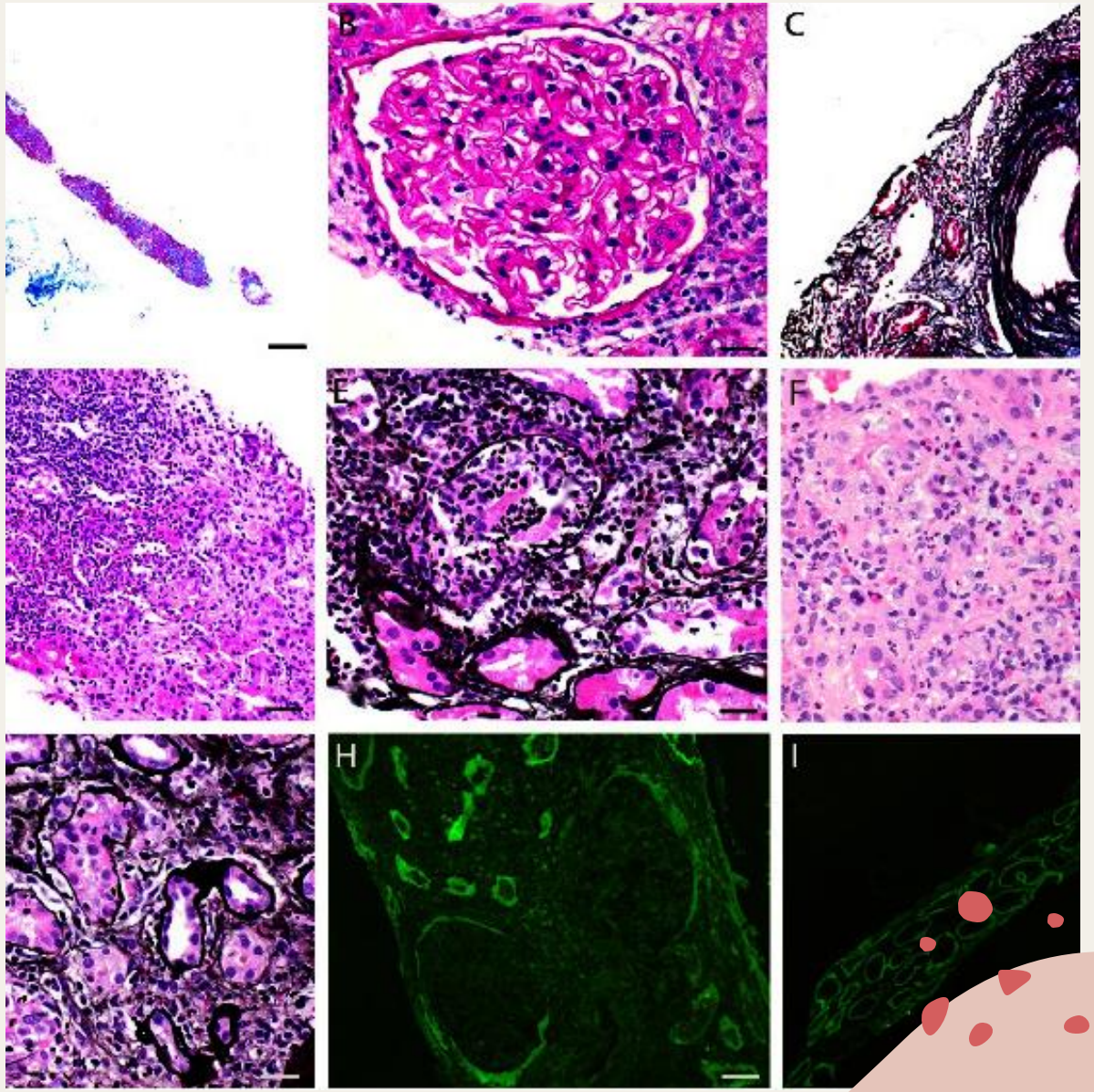
Differential diagnosis that I thought

- med effects, no NSAID's or diuretics, no new meds since May, no IV contrast
- renovascular-ruled out by doppler
- lupus nephritis though no protein in urine and trace RBC, neg dsDNA
- scleroderma renal crisis though normotensive
- amyloidosis from long term RA
- something new like vasculitis, infection but no other symptoms

A diagnostic study was performed

Renal biopsy results

Acute interstitial nephritis (AIN) with anti-tubular basement membrane antibody staining. Staining was more granular than linear (atypical).



Anti tubular basement membrane (TBM)disease

Rare disease that causes acute renal failure

Can be associated with acute interstitial nephritis

Genetic forms also exist, mostly associated with membranous nephropathy

Can occur with other autoimmune diseases

Unlike anti GBM/Goodpasture's disease, does not have pulmonary symptoms

Potential causes of anti TBM with AIN

- Drugs, most reports as immune related adverse events of cancer immunotherapies

  Nivolumab +/- ipo mostly commonly reported for renal cell carcinoma

- Genetic
- Other autoimmune diseases

  case report of Sjogren's with MGUS and anti TBM JASN 2024 poster

Causes of acute interstitial nephritis

- Drugs – 70 to 75 percent (with antibiotics responsible for approximately 30 to 50 percent of these cases)
- Systemic disease including sarcoidosis, Sjogren's disease, systemic lupus erythematosus (SLE), and others – 10 to 20 percent
- Infections – 4 to 10 percent
- Tubulointerstitial nephritis and uveitis (TINU) syndrome – less than 5 percent

Drugs associated with interstitial nephritis

Common drugs that cause AIN include:

- Nonsteroidal antiinflammatory agents (NSAIDs), including selective cyclooxygenase (COX)-2 inhibitors
- Penicillins and cephalosporins (methicillin is the classic one but no longer on the market)
- Rifampin
- Antimicrobial sulfonamides, including trimethoprim-sulfamethoxazole
- Ciprofloxacin and, perhaps to a lesser degree, other quinolones
- Diuretics, including loop diuretics such as furosemide and bumetanide, and thiazide-type diuretics
- Cimetidine (only rare cases have been described with other H-2 blockers such as ranitidine)
- Allopurinol
- Proton pump inhibitors (PPIs) such as omeprazole and lansoprazole
- 5-aminosalicylates (eg, mesalamine)
- Anticancer drugs, such as immune checkpoint inhibitors (ICPi; such as ipilimumab and nivolumab)

Follow up

- Turns out she had Clindamycin course started on 10/28 and Penicillin on 11/20
- She is currently on 80 mg of prednisone (diagnosis made 1/15/25)
- Follow up creat was 4.69, down from 4.8, after she had the lower dose steroids for arthritis
- Creat 3.7 on 1/22 after more steroids, still with uremic symptoms
- Received her actual biopsy report on 1/22 and it says chronic interstitial nephritis with quite a bit of fibrosis
- We are planning on stopping her sarilumab and switching to rituximab, not due to concern for sarilumab toxicity but for better control of antibody formation
- She is off Omeprazole now and switching her off Losartan
- Any ideas for further workup or treatment options are welcomed!

Take home messages

- Think of anti TBM with AIN in patients with acute renal failure even in the absence of urine eosinophils (my patient had no WBC in the urine)
- Mostly caused by drugs like antibiotics, NSAID's and cancer immunotherapy
- Treatment is removal of the offending agent, steroids and immunosupressants. Most often used are mycophenolate, cyclophosphamide.

A couple Helene photos