Clinical and histological features of COVID-19 associated glomerular disease

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Disclosures

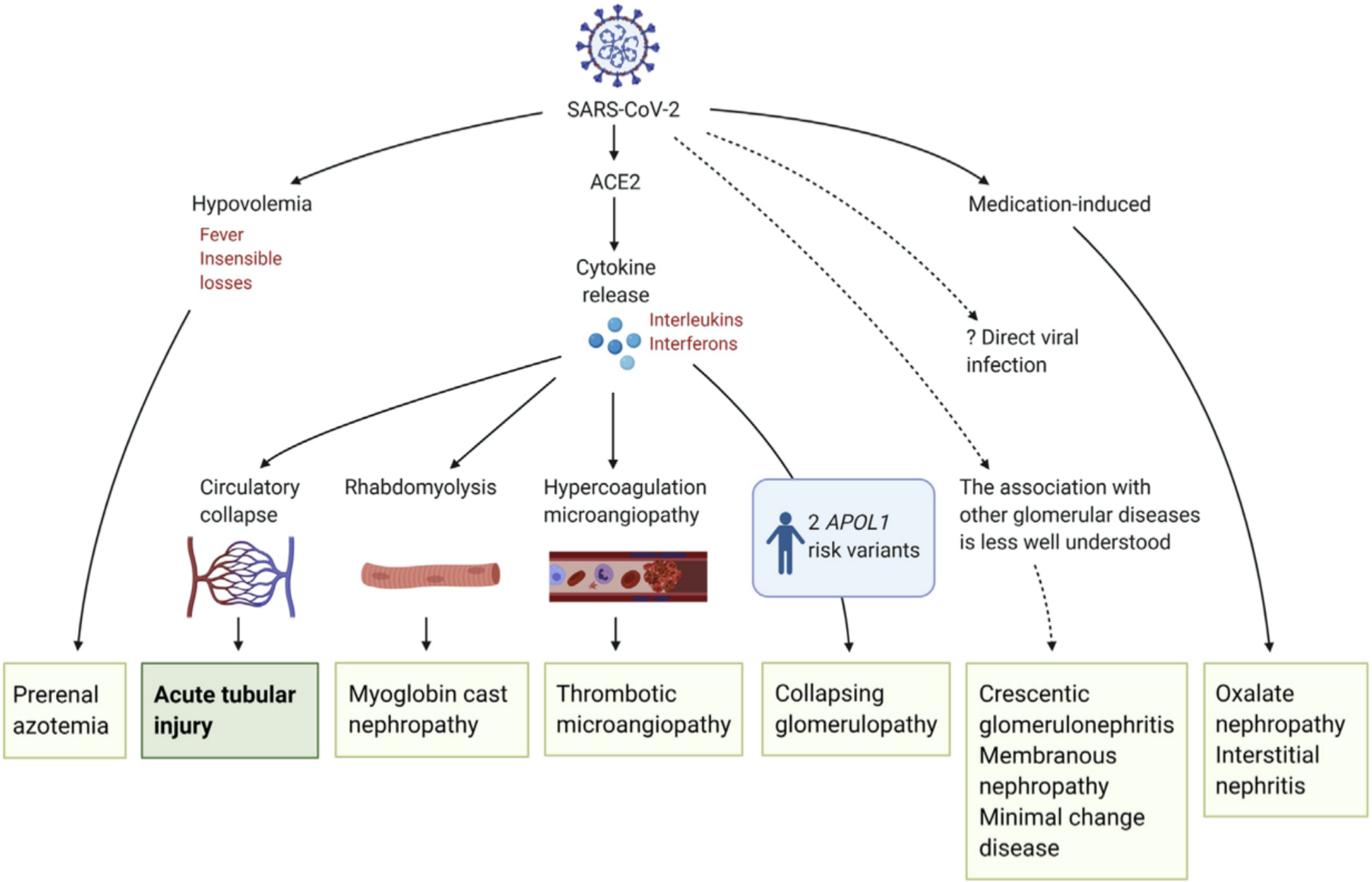
- None

Objectives

1. To describe the clinical and histological features of podocytopathies associated with COVID-19

2. To review the clinical and histological features of COVID-19 associated thrombotic microangiopathy (TMA)

3. To discuss immune-mediated glomerular diseases reported in patients with COVID-19



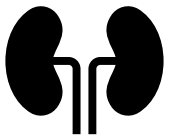
Ng JH, Bijol V, Sparks MA et al Pathophysiology and Pathology of Acute Kidney Injury in Patients With COVID-19. Adv Chronic Kidney Dis. 2020 Sep;27(5):365-376

Diverse kidney biopsy findings reported in patients with COVID-19

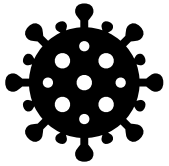
Setting

8 large referral centers in the U.S.
N=34

Median age 54
20 male, 14 female
20 Black race



28 native, 6 allograft



Clinical Presentation

65% with *mild* COVID-19 symptoms

Kidney disease manifested within 1 week of COVID-19

<u>Biopsy indications</u>
88% AKI
60% Nephrotic range proteinuria/nephrotic syndrome

Pathological findings

Acute tubular necrosis - 56%
Podocytopathy - 41%
- Collapsing glomerulopathy
- Minimal change disease

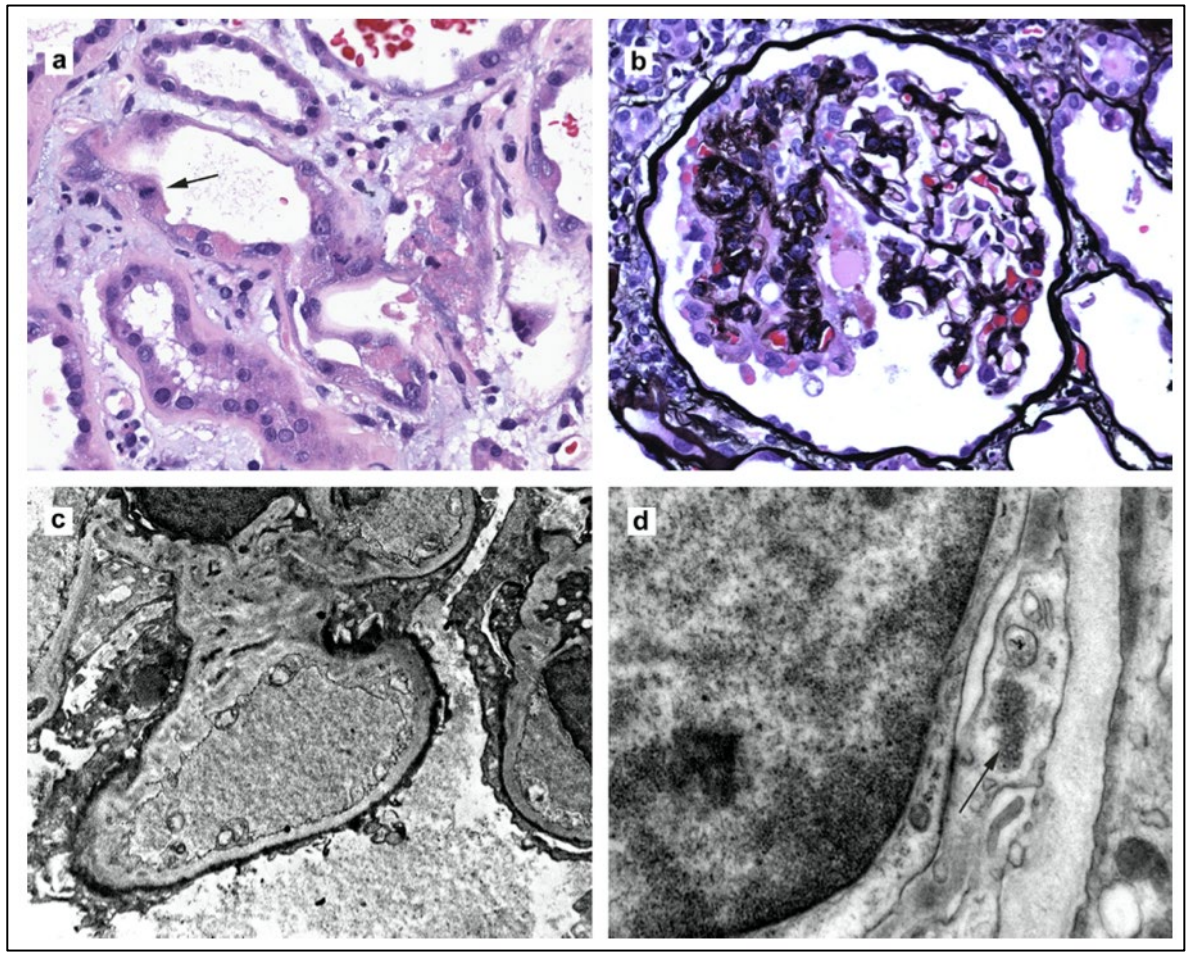
Thrombotic microangiopathy - 18%
Immune-mediated glomerular diseases - 12%
- Membranous nephropathy
- Lupus nephritis
- Anti-GBM nephritis
- Infectious GN

Kudose S, Batal I, Santoriello D et al Kidney Biopsy Findings in Patients with COVID-19. J Am Soc Nephrol. 2020 Sep;31(9):1959-1968
Akilesh S, Nast CC, Yamashita M et al Multicenter Clinicopathologic Correlation of Kidney Biopsies Performed in COVID-19 Patients Presenting With Acute Kidney Injury or Proteinuria. Am J Kidney Dis. 2021 Jan;77(1):82-93.e1

Podocytopathies associated with COVID-19

April 9, 2020
First reported case of COVID-19 associated CG

- 44-year-old African American woman presented with fever, worsening cough and was diagnosed with COVID-19
- Found to have SCr 4.0 mg/dL and nephrotic range proteinuria of 3.9g
- At least 32 reported cases of CG associated with COVID-19 to date



Larsen CP, Bourne TD, Wilson JD et al Collapsing Glomerulopathy in a Patient With COVID-19. Kidney Int Rep. 2020 Apr 9;5(6):935-939

COVID-19 associated CG

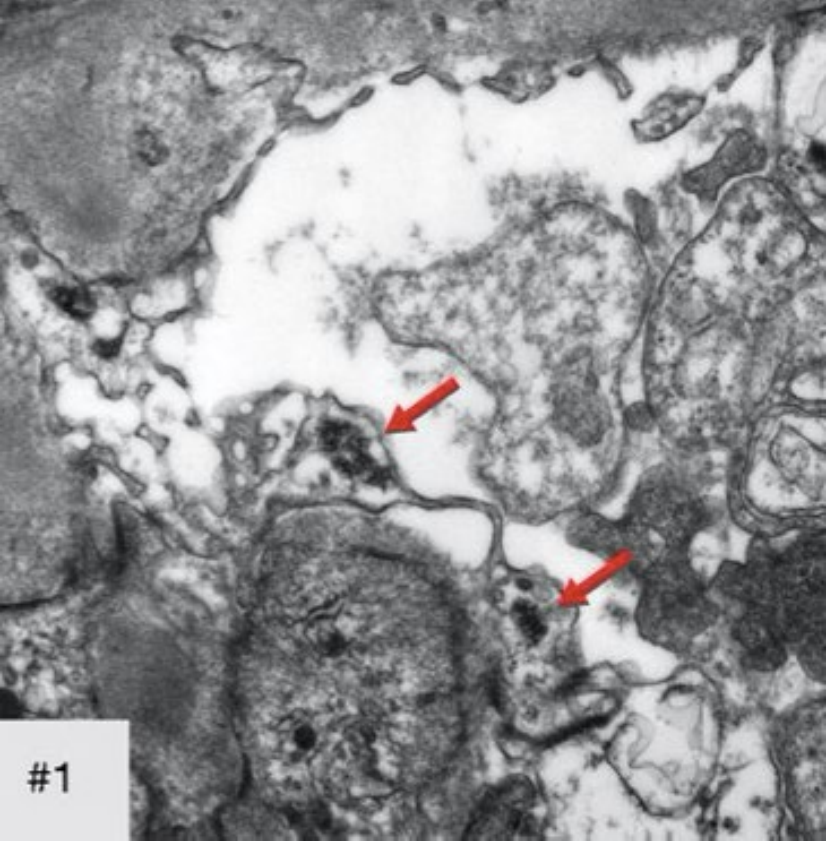
- 100% present with AKI and proteinuria, typically nephrotic range
- Kidney injury >> respiratory symptoms
- Majority (96%) of African ancestry
- High risk *APOL1* genotype found in 100% cases tested

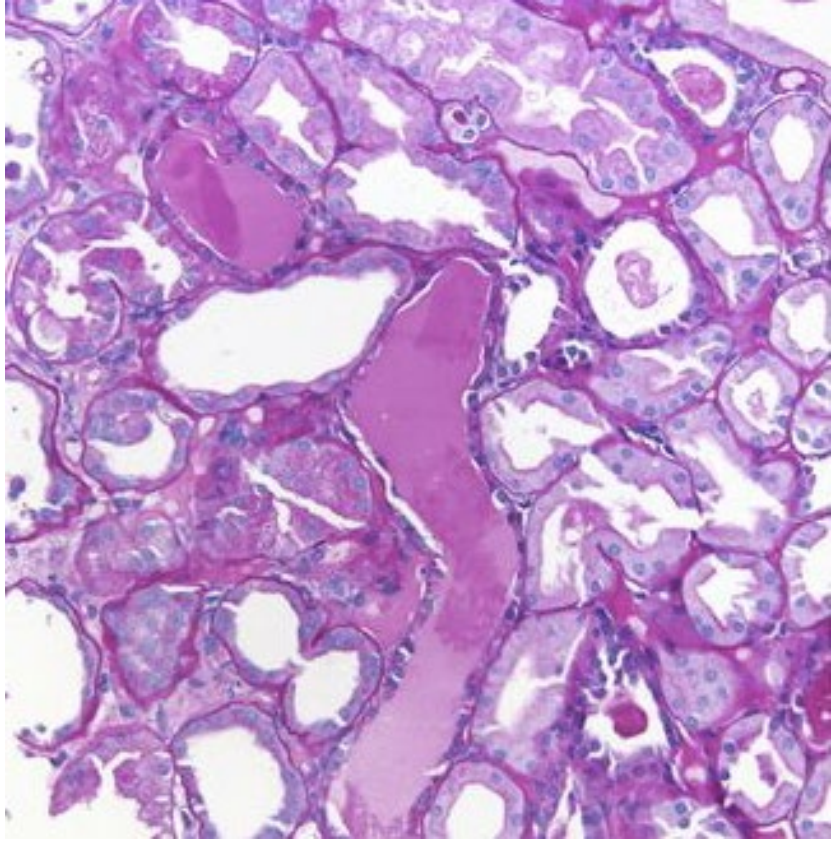
  → G1/G1, G1/G2, G2/G2
- Treatment in most supportive

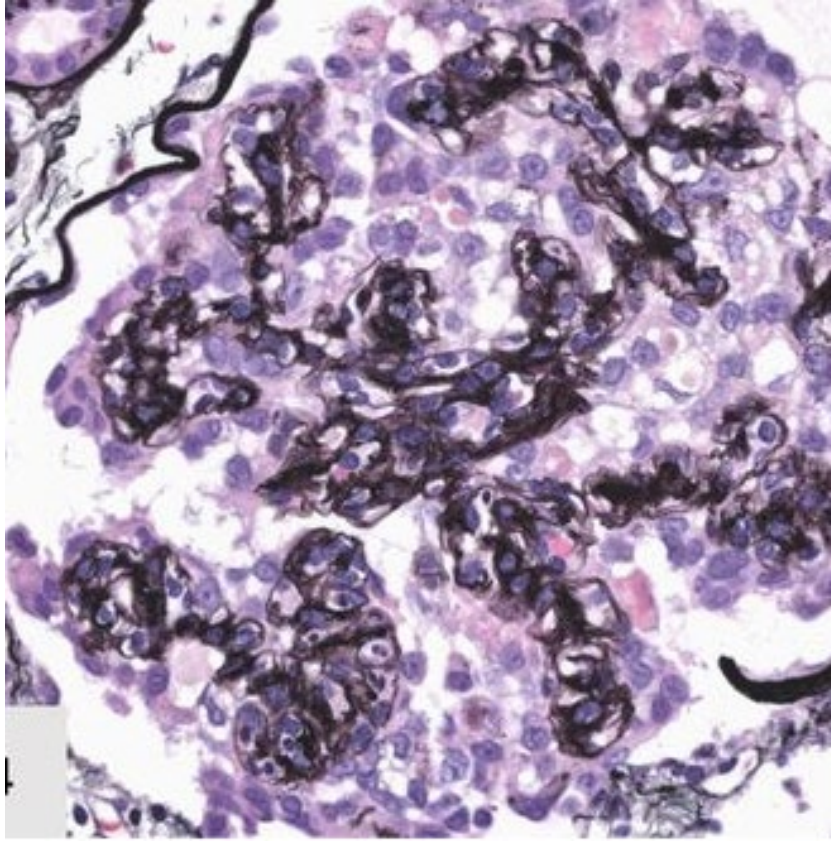
  → >50% require kidney replacement therapy

  → Many recover kidney function after 40-90 day follow up

Wu H, Larsen CP, Hernandez-Arroyo CF et al AKI and Collapsing Glomerulopathy Associated with COVID-19 and *APOL1* High-Risk Genotype. J Am Soc Nephrol. 2020 Aug;31(8):1688-1695
Shetty AA, Tawhari I, Safar-Boueri L et al COVID-19-Associated Glomerular Disease. J Am Soc Nephrol. 2021 Jan;32(1):33-40
Kudose S, Batal I, Santoriello D et al Kidney Biopsy Findings in Patients with COVID-19. J Am Soc Nephrol. 2020 Sep;31(9):1959-1968







Histological features of COVID-19 associated CG

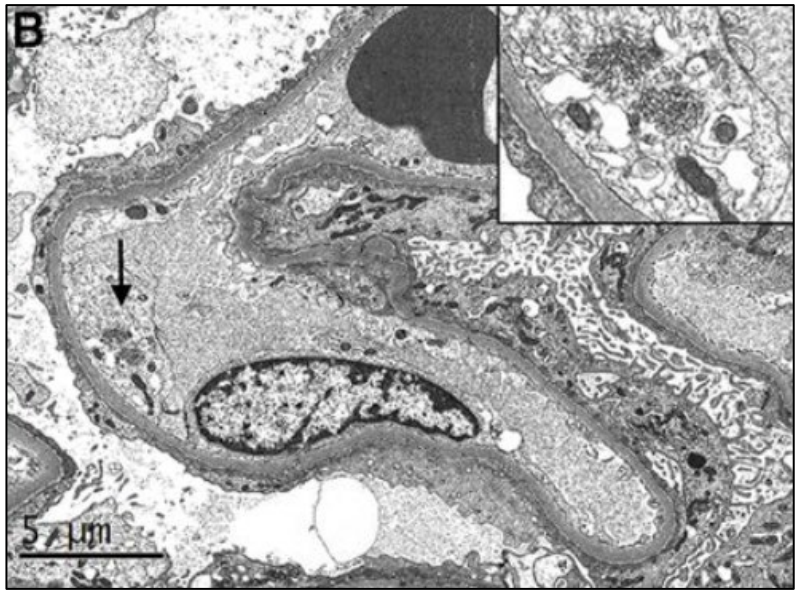
- Acute tubular injury, microcystic tubules
- Glomerular tuft collapse
- Parietal epithelial cell hypertrophy and hyperplasia
- Extensive foot process effacement
- Tubuloreticular inclusions

Wu H, Larsen CP, Hernandez-Arroyo CF et al AKI and Collapsing Glomerulopathy Associated with COVID-19 and *APOL1* High-Risk Genotype. J Am Soc Nephrol. 2020 Aug;31(8):1688-1695

Other podocytopathies associated with COVID-19

- **Minimal change disease** – 2 cases
  → 1 patient with high risk *APOL1* genotype
  → Concurrent COVID-19 and new-onset nephrotic syndrome
  → Treatment with prednisone → remission after ~4 weeks

- **Non-collapsing focal segmental glomerulosclerosis**



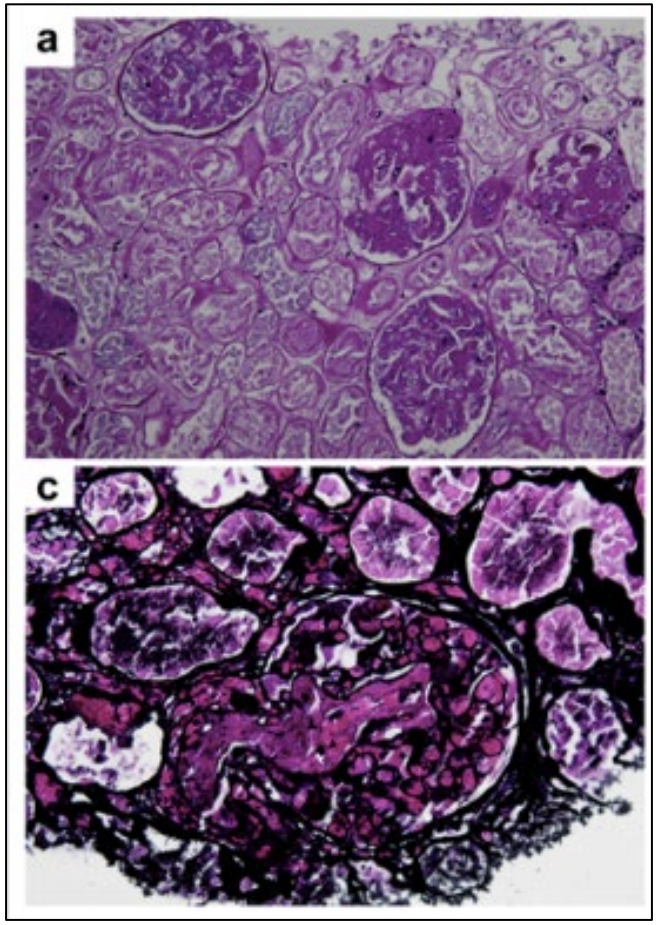
Sharma P, Ng JH, Bijol V et al Pathology of COVID-19-associated acute kidney injury. Clin Kidney J. 2021 Jan 24;14(Suppl 1):i30-i39

COVID-19 associated TMA

Case report – Thrombotic microangiopathy associated with COVID-19

69-year-old female presented with cough and fevers was found to have COVID-19 pneumonia

	Day 1	Day 7	Day 16	Day 17	Day 18	Day 19	Day 20	Day 21
Treatment given	Hydroxychloroquine/ low-molecular-weight heparin	Anakinra & tocilizumab	Convalescent plasma	Intubation	Dialysis started		Kidney biopsy	Eculizumab
Hemoglobin (11.5–15.5 g/dl)	13	11.5	12.9	11.8	8.0	8.3	8.6	6.9
Platelets (150–400 K/ul)	203	142	85	14	97	37	21	27
Serum creatinine, mg/dl	0.72	0.75	0.57	2.06	2.49	4.07	On dialysis	On dialysis
Fibrinogen (350–510 mg/dl)				62	159	128	117	166
D-dimer (<229 ng/ml DDU)	411				6068	14,568	12,193	5927
ADAMTS 13 activity level (>66.8%)					43.2			
Alkaline phosphatase (40–120 U/l)	137	118	292	296	194	212	204	294
AST (10–40 U/l)	70	44	63	316	404	254	173	148
ALT (10–45 U/l)	38	30	27	97	146	239	230	165
LDH (50–242 U/l)	459		1073		3518	5130	5183	4707
C-reactive protein (0–0.40 mg/dl)	10.35	2.46	6.85		18.54	20.73	13.61	8.02
Hep- PF 4 AB result (0.0–0.9 U/ml)			<0.6					
Hep- PF 4 AB interpretation			Negative					
Schistocytes in smear					Present	Present		
Haptoglobin (34–200 mg/dl)					<20	<20		

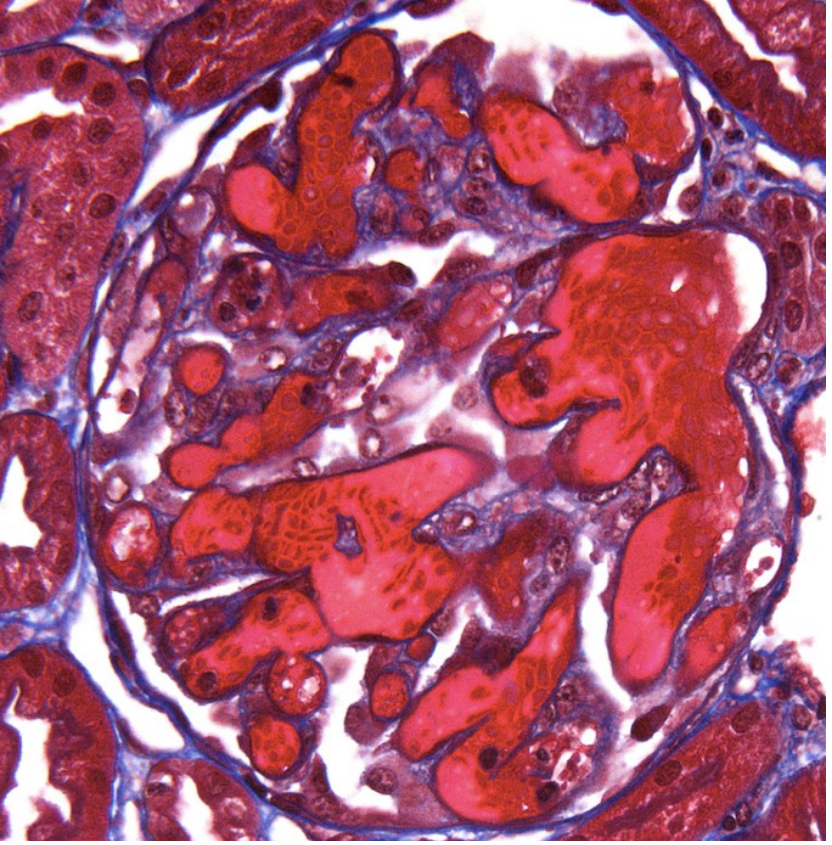


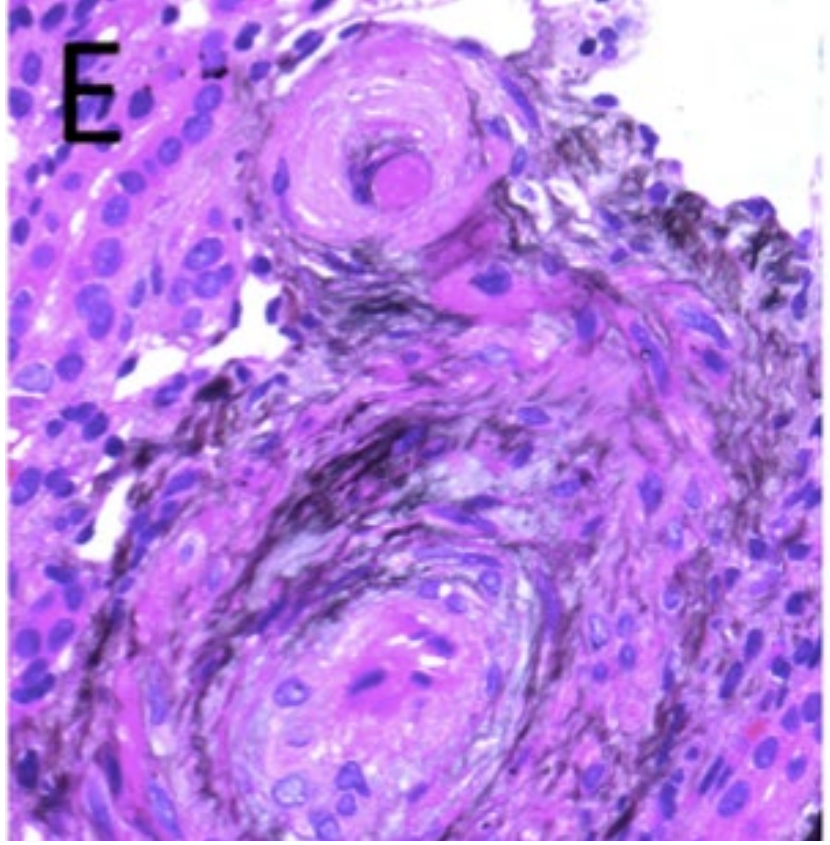
Jhaveri KD, Meir LR, Flores Chang BS et al Thrombotic microangiopathy in a patient with COVID-19. Kidney Int. 2020 Aug;98(2):509-512

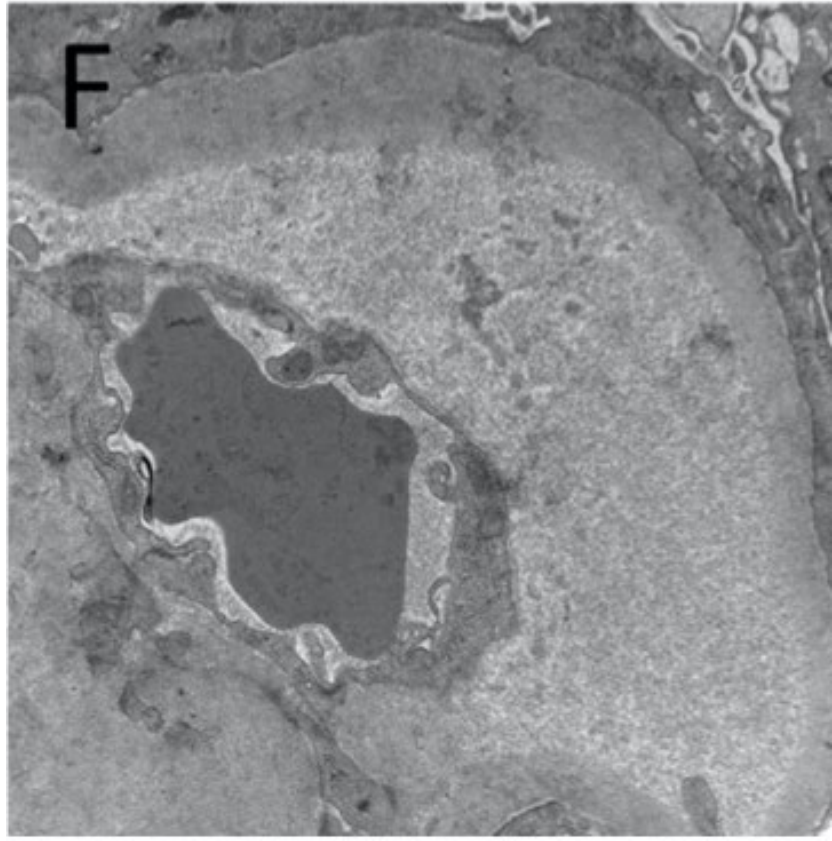
COVID-19 associated TMA

- Associated with severe SARS-CoV-2 infection
- Resembles complement-mediated TMA
  - → AKI, variable proteinuria, severe hypertension (BP >160/100 mmHg)
  - → Thrombocytopenia, microangiopathic anemia with normal PT/PTT
- Predisposing risk factors often present
  - →Drugs (i.e. gemcitabine), hypertension, genetic predisposition
- Majority treated with supportive care - select few given eculizumab
  - → 100% of 9 cases required kidney replacement therapy
  - → >50% mortality

Sharma P et al Northwell Nephrology COVID-19 Research Consortium. COVID-19-Associated Kidney Injury: A Case Series of Kidney Biopsy Findings. J Am Soc Nephrol. 2020 Sep;31(9):1948-1958
Akilesh S, et al Multicenter Clinicopathologic Correlation of Kidney Biopsies Performed in COVID-19 Patients Presenting With Acute Kidney Injury or Proteinuria. Am J Kidney Dis. 2021 Jan;77(1):82-93.e1





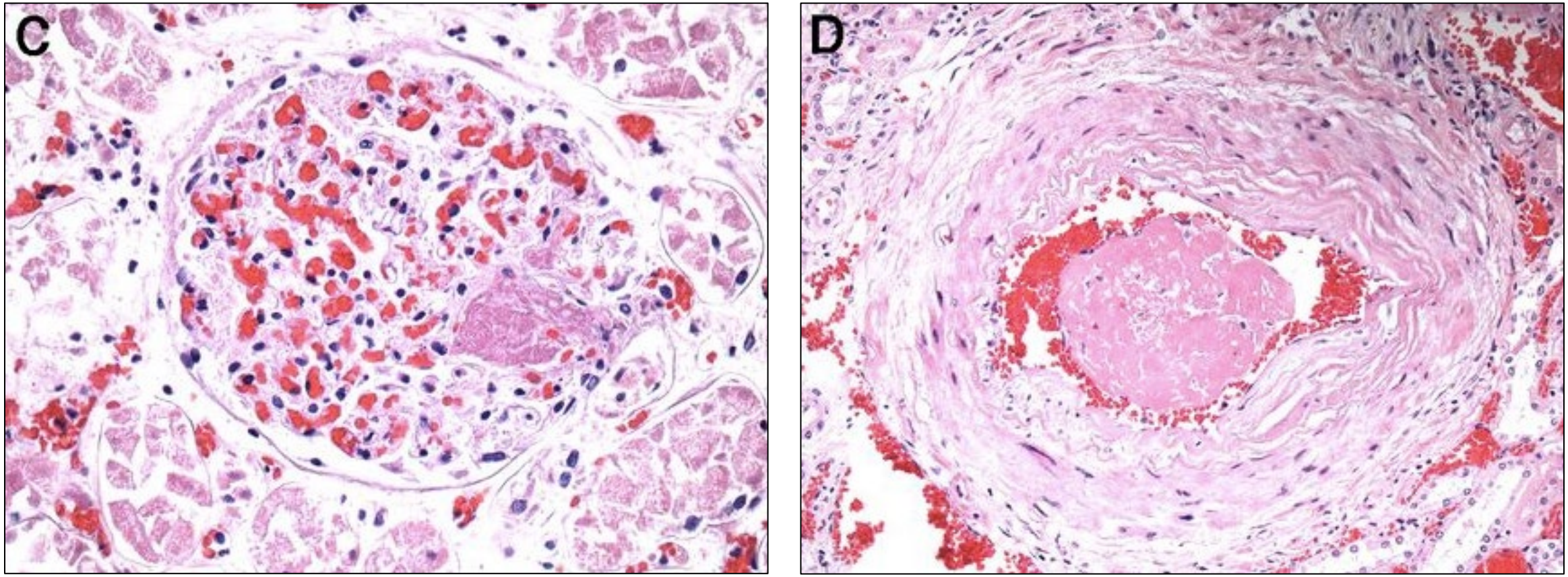


Histological features of COVID-19 associated TMA

- Primary finding or seen with ATN or CG
- Glomerular and arteriole thrombi
- Fibrin deposits in capillary lumens
- Subendothelial space expansion, duplication of GBM

Akilesh S, Nast CC, Yamashita M et al Multicenter Clinicopathologic Correlation of Kidney Biopsies Performed in COVID-19 Patients Presenting With Acute Kidney Injury or Proteinuria. Am J Kidney Dis. 2021 Jan;77(1):82-93.e1; Left picture with permission from Dr. Cynthia Nast, Director of Renal Pathology at Cedars Sinai

Focal thrombi in glomeruli and renal arterioles observed in 15% post-mortem cases



Santoriello D, Khairallah P, Bomback AS et al. Postmortem Kidney Pathology Findings in Patients with COVID-19. J Am Soc Nephrol. 2020 Sep;31(9):2158-2167

Immune-mediated glomerular diseases in patients with COVID-19

Variety of immune-mediated glomerular diseases reported in patients with COVID-19

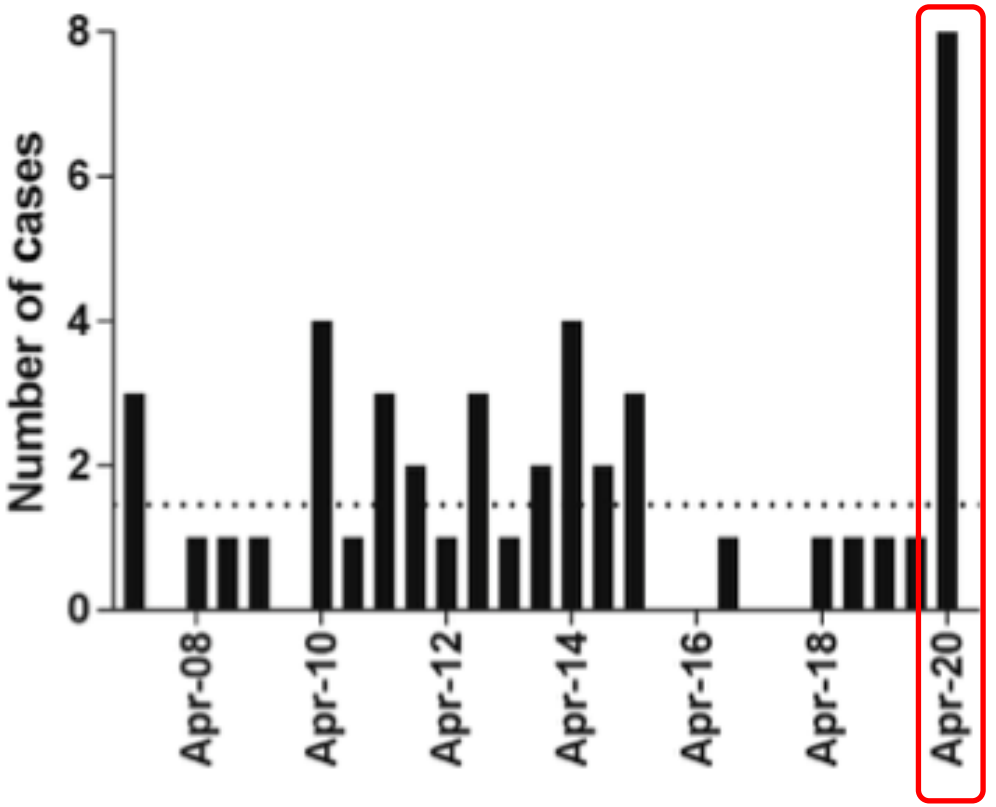
- Cytokine storm → altered response to SARS-CoV-2 and autoimmunity

Anti-GBM disease – 6 cases
ANCA-associated vasculitis – 4 cases
IgA nephropathy – 2 cases
Infectious-glomerulonephritis – 1 case
Membranous nephropathy – 2 cases
Crescentic transformation of class II lupus nephritis – 1 case

Sharma P, Ng JH, Bijol V et al Pathology of COVID-19-associated acute kidney injury. Clin Kidney J. 2021 Jan 24;14(Suppl 1):i30-i39
Kant S, Raman G, Damera P, et al Characteristics and Outcomes of COVID-19 in Patients With Antineutrophil Cytoplasmic Antibody-Associated Vasculitis. Kidney Int Rep. 2021 Mar;6(3):806-809
Huang Y, Li XJ, Li YQ et al Clinical and pathological findings of SARS-CoV-2 infection and concurrent IgA nephropathy: a case report. BMC Nephrol. 2020 Nov 24;21(1):504

Anti-GBM disease

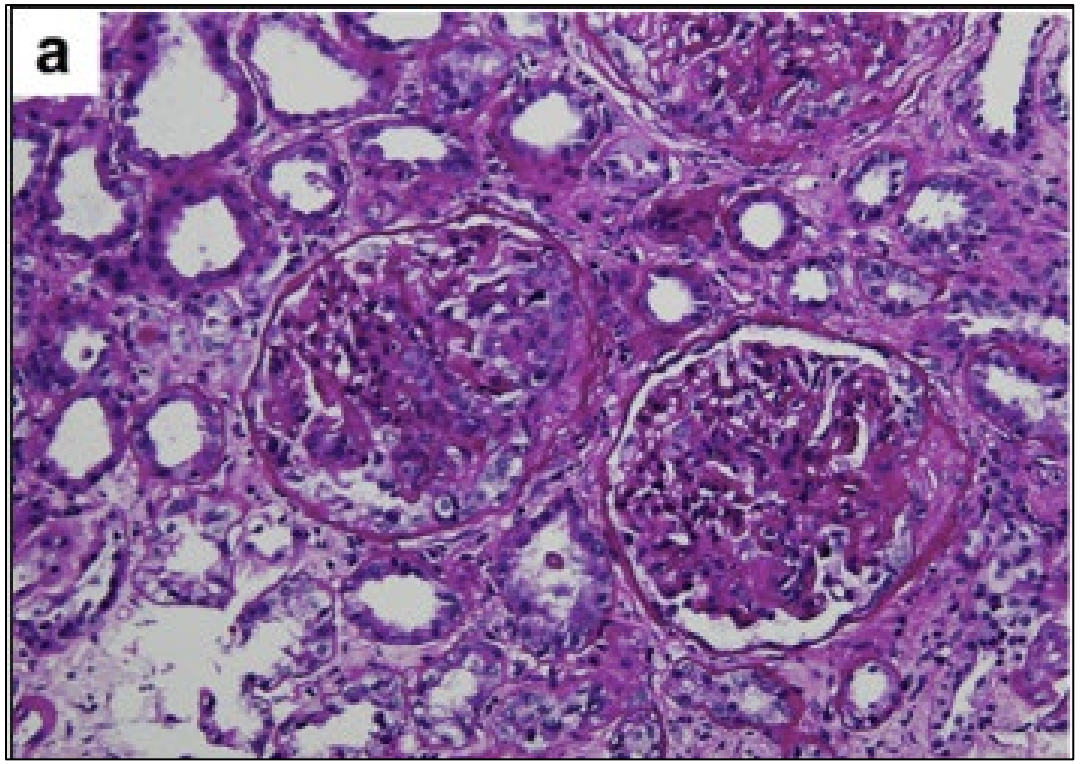
- First described during Spanish flu in 1919
- 5-fold ↑ from December 2019-April 2020 in London, UK
- URI and/or diarrheal illness 1-8 weeks preceding diagnosis
- 50% IgM and/or IgG SARS-CoV-2 Abs
- All treated with PLEX, steroids, cyclophosphamide
- >50% required KRT but half recovered kidney function



Prendecki M, Clarke C, Cairns T et al Anti-glomerular basement membrane disease during the COVID-19 pandemic. Kidney Int. 2020 Sep;98(3):780-781

ANCA-associated vasculitis

	Patient 1	Patient 2	Patient 3	Patient 4
Age/gender Ethnicity	64M African	46M South Asian	25M -	37F Iranian
ANCA	MPO	PR3	PR3	PR3
Symptoms	COVID-19 pneumonia	COVID-19 pneumonia	Pulmonary hemorrhage	Pulmonary hemorrhage
Biopsy	←Crescentic glomerulonephritis→			-
Induction	Steroids + RTX	Steroids + RTX	PLEX + steroids + CYC	PLEX + steroids



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Summary

- Podocytopathies are the most common form of glomerular disease reported in patients with COVID-19.

- COVID-19 associated CG is strongly associated with high risk *APOL1* genotype. Studies are needed to evaluate the risk of CKD progression in this population following SARS-CoV-2 infection.

- TMA is associated with severe SARS-CoV-2 infection and is often observed in individuals with a predisposing risk factor.

- The inflammatory milieu observed in SARS-CoV-2 infection may trigger or exacerbate immune-mediated glomerular diseases in susceptible individuals.